

ETS: RESPIRATORY  
DISEASES AND  
CONDITIONS IN  
NONSMOKING  
ADULTS AND  
CHILDREN

VOLUME V

9/93

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THIS ISSUE BINDER IS INTENDED TO PROVIDE A BASIC,  
COMPREHENSIVE REVIEW OF THE SCIENTIFIC LITERATURE  
REGARDING A SPECIFIC TOPIC ON ETS AND THE HEALTH OF  
NONSMOKERS.

PRIMARY STUDIES AND REVIEWS HAVE BEEN HIGHLIGHTED  
TO IDENTIFY (1) USEFUL OR HELPFUL INFORMATION (YELLOW  
HIGHLIGHT) AND (2) ADVERSE RESULTS OR OPINIONS (BLUE  
HIGHLIGHT) .

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**2023510095****CONFOUNDERS**

## CONFOUNDERS

Studies on parental smoking and childhood respiratory disease rarely address confounding variables. Confounding variables are factors that can create a "false" association between two elements by being associated with one or both of them. For example, factor X (socioeconomic status) may be associated with both factor Y (parental smoking) and factor Z (childhood respiratory disease). When factor X is not controlled for in epidemiological studies of the possible association between factor Y and factor Z, a false association may appear between factors Y and Z. Therefore, it is vital that epidemiologists control for confounding variables when conducting studies such as those on parental smoking. The possible confounding variables associated with parental smoking and childhood respiratory disease can be grouped into four major categories: (1) household heating and cooking sources; (2) outdoor air pollution; (3) organic substances; and (4) demographic, medical and socioeconomic factors.

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### Household heating and cooking sources

Children living in households with gas stoves have been reported to have a greater history of respiratory illness before the age of two and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height<sup>1</sup> (FEV<sub>1</sub> and FVC are standard measurements of lung capacity and function). Similarly, exposure of children to gas cooking in the first two years of life has been associated with an increased risk of hospitalization for respiratory illness<sup>2</sup>. There are reported associations of gas stove use with daily peak flow in asthmatic, normal, and allergic subjects.<sup>3</sup>

Oxides of nitrogen (NO<sub>x</sub>) arising from the use of gas stoves for cooking were proposed to be related to a reported increase in cough, "colds going to the chest," and bronchitis in a study of 5,758 English and Scottish children aged six to eleven years<sup>4</sup>. A number of other confounders were controlled for in this study, including "age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating." One group of researchers reported similar results for a five-year longitudinal study of 4827 boys and girls, ages five to ten years. This reported association was independent of age, sex, social class, number of cigarette smokers in the home, and latitude, and was only found in urban areas.<sup>5</sup>

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Use of unvented kerosene heaters, which release nitrogen dioxide ( $\text{NO}_2$ ) into the indoor environment, was associated with significantly more days of acute respiratory illness in exposed children<sup>6</sup>. In this study, there was no difference in the number of cigarettes smoked daily in the homes of exposed versus unexposed children.  $\text{NO}_2$  exposure was also reported to be associated with a risk of reporting lower respiratory symptoms in children under the age of seven<sup>7</sup>.

One study reported increased proportions of chest illnesses and hospitalizations for chest illness before age two in young children living in homes heated by wood-burning stoves. Medical histories, sociodemographic factors, or exposure to other pollutant sources did not account for the reported association<sup>8</sup>.

In another report, hot water heating systems were reported to have a large effect on lung function in children, when compared to the use of forced air heating and air conditioning systems<sup>9</sup>.

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### Outdoor air pollution

Outdoor air pollutants have been identified as a confounder in several studies. In one study, acute respiratory disease incidence was reported to be positively associated with higher ambient sulfate levels<sup>1</sup>.

A group of researchers examined the importance of indoor and outdoor environmental factors (parental smoking, gas cooking, suspended particulates and sulfur dioxide) in the respiratory health of seven- to ten-year-old Canadian children. The researchers were unable to identify any effects of parental smoking or gas cooking because the prevalence of these variables was highest in an industrial area of high particulate pollution<sup>2</sup>.

One researcher has reported a strong association between respiratory illness and particulate pollution in children living in a study site which experiences relatively high levels of particulate pollution<sup>3</sup>.

A study comparing Israeli children living in a polluted industrial town versus those living in an unpolluted area reported that chronic respiratory symptoms and most pulmonary diseases were significantly more common among those children from the polluted town<sup>4</sup>.

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### Organic substances

The relevance of home dampness in the etiology of respiratory symptoms in children is supported by current research which links dampness with the presence of molds, dust mites, fungi and other allergenic microbes.

In one study, odds ratios of 1.23 and 2.16 were reported for home dampness after adjustment for several factors, including maternal smoking, in a cohort study of 4,625 eight- to twelve-year-old children living in six United States cities<sup>1</sup>. The authors reported odds ratios for molds of 1.27 to 2.12 after adjustment for maternal smoking and several other factors.

Another study reported higher rates of respiratory symptoms and symptoms of infection and stress among children living in damp houses. The presence of "fungal mould" was also reported to be related to higher rates of respiratory symptoms, independent of smoking in the household<sup>2</sup>. In another study, the growth of fungi and molds in the home was directly related to respiratory symptoms and sensitization to common allergens in children<sup>3</sup>.

Researchers have reported that children living in damp and moldy dwellings had a greater prevalence of respiratory symptoms and headache and fever than those living in dry homes. The authors reported a dose-response relationship with increasing

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numbers of symptoms reported in dwellings with higher severity of dampness and mold. All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding<sup>4</sup>.

Atopic sensitization of children to house dust mites was reported to be related to home dampness<sup>5</sup>.

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### Demographic, medical and socioeconomic factors

Low socioeconomic status has been associated with an increased incidence of respiratory complications<sup>1</sup>. Factors related to lower socioeconomic status include: inadequate medical care, poor nutrition, poor outdoor air quality, increased parental coughing, higher gas stove usage, frequent change of address, and lower per capita living space. In a study of 1,050 European children aged eight and nine years, lifetime and current prevalence of wheeze were both significantly higher in children from low socioeconomic status<sup>2</sup>.

Watkins, et al., (1986) reported high consultation rates for respiratory illness in children whose fathers were in manual occupations. This association was not explained by crowded home conditions or parental smoking<sup>3</sup>. Gardner, et al., (1984) reported significantly higher rates of lower respiratory disease in infants of low socioeconomic status<sup>4</sup>.

Cross-infection also plays a role in the incidence of children's respiratory disease. For instance, in a 1988 paper, Koo, et al., reported that among Japanese and Hong Kong Chinese women, there was a highly significant correlation between the frequency of maternal respiratory illness and the frequency of respiratory illness in her children<sup>5</sup>.

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Cross-infection may be relevant to the reports of associations between day care attendance and respiratory illness. Anderson, et al., (1988) reported that care outside the home (day care) is an important factor for acquiring lower respiratory tract illness and infectious diseases in children under two years of age<sup>6</sup>. Gardner, et al., (1984) also noted significantly higher rates of lower respiratory disease among day care infants<sup>4</sup>. Fleming, et al., (1987) reported an increased risk for upper respiratory tract infection associated with day care attendance<sup>7</sup>.

Familial characteristics and genetics may also act as confounders. For instance, in a 1982 publication, Lebowitz, et al., report that an observed relationship between children's pulmonary function and parental smoking disappeared when household aggregation of body mass was taken into account<sup>8</sup>. Another Lebowitz, et al., study (1984) also reported that there was "no remaining independent aggregation of pulmonary function measurements" after familial aggregation of body habitus was controlled for<sup>9</sup>. Genetic predisposition may play a role in respiratory illness and pulmonary function<sup>10</sup>; although cross-infection is also involved<sup>11</sup>.

"Lifestyle" may also act as a confounder. A study in Copenhagen (Holma and Winding, 1977) examined 109 social, medical, housing, and hygiene factors on morbidity. The best predictors for health were "thriving" (satisfaction), followed by "housing standard" and "personal hygiene." The authors reported no effect

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of parental cigarette smoking on the respiratory health of young children<sup>12</sup>. A survey of 314 nonsmoking Hong Kong Chinese women and their children and 243 Japanese women and their children reported that chronic cough and sputum symptoms were at least 10 times more prevalent in Hong Kong<sup>5</sup>. This observation was attributed to occupational exposure to dust or fumes and household crowding among the Hong Kong mothers.

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**PARENTAL SMOKING: CONFOUNDING VARIABLES**

Access to medical care  
Age of mother  
Air pollution  
Birth weight  
Breast feeding  
Cooking practices/type  
Day care attendance  
Diet  
Family history of illness  
Family size  
Gender of child  
Genetic determinants  
Heating type  
Home dampness  
Hospital spread of illness  
Household pets  
Newborn illnesses  
Nurture  
Overcrowding  
Parental education  
Parental infections  
Place of residence  
Seasonal variation  
Skin test reactivity (allergy)  
Socioeconomic status

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Colley, J.R.T. "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production" British Medical Journal 2: 201-204, 1974.

SUMMARY: A study of respiratory symptoms in 2,426 school children aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with the parents' smoking habits; prevalence was lowest where both parents were non-smokers, highest where both parents smoked, and lay between these two levels where only one parent smoked. A close association was found between parents' and childrens' respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents smoke, is an important element in the association.

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## Discussion

Despite the increase in our knowledge and understanding of the pathogenic mechanisms present in patients with diffuse toxic goitre—particularly since the discovery of LATS (Adams, 1958) and its characterization as an immunoglobulin (Adams and Kennedy, 1962; McKenzie, 1962; Kriss *et al.*, 1964; Dorrington *et al.*, 1966)—the cause of the abnormal thyroid function in this disease has remained uncertain. The simplest explanation, and the only one which accounts for the phenomenon of neonatal thyrotoxicosis, is that there is a circulating humoral stimulator acting upon the gland (McKenzie, 1972). Thyrotrophin has been excluded from this role by the fact that its level in blood is less than normal in diffuse toxic goitre (Adams *et al.*, 1969). To many workers LATS has been unacceptable as a causative agent because it is undetectable in many cases and the level in any individual patient does not correlate with the degree of abnormal thyroid function (Volpe *et al.*, 1972). LATS protector, however, meets two criteria not fulfilled by LATS; our evidence confirms the high incidence of LATS protector in diffuse toxic goitre and shows that its serum level correlates well with early thyroid <sup>131</sup>I uptake. Furthermore, LATS protector has been shown to stimulate the human thyroid, both *in vitro* (Shishiba *et al.*, 1973) and *in vivo* (Adams *et al.*, 1974). We therefore think that in LATS-negative patients with diffuse toxic goitre LATS protector is the pathogenic agent.

The question whether LATS protector is present in every case of diffuse toxic goitre remains open. It was not found in five of the 50 patients studied, but all these were relatively mild cases with normal or only slightly raised thyroid <sup>131</sup>I uptake and large goitres. Failure to detect LATS protector in these inactive cases may have been due to assay insensitivity, but incorrect diagnosis of thyrotoxicosis or an alternative pathogenic mechanism for thyroid dysfunction are other possible explanations.

The pathogenesis of the ophthalmopathy of Graves's disease remains less well understood than the pathogenesis of thyrotoxicosis. We found no significant correlation between the class of ophthalmopathy and the LATS protector level. The highest incidence of infiltrative ophthalmopathy, however, was observed in the group of patients with both LATS and LATS protector, and the lowest incidence was in those patients in whom neither immunoglobulin could be detected. Our findings support the view that LATS protector and ophthalmopathy may be associated in Graves's disease but the relation is not a causal one.

We thank Mr. W. S. Cagge for skilled technical help.

Requests for reprints should be addressed to Dr. R. D. H. Stewart.

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# Respiratory Symptoms in Children and Parental Smoking and Phlegm Production

J. R. T. COLLEY

*British Medical Journal*, 1974, 2, 201-204

## Summary

A study of respiratory symptoms in 2,426 schoolchildren aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with the parents' smoking habits; prevalence was lowest where both parents were non-smokers, highest where both parents smoked, and lay between these two levels where only one parent smoked. A close association was found between parents' and children's respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents smoke, is an important element in the association.

## Introduction

Norman-Taylor and Dickinson (1972) suggested that children with parents who smoke may be at particular risk from respiratory disease. These authors were not, however, explicit about the nature of the risk. They implied that exposure of children to cigarette smoke at home might increase the risk of respiratory illness. This paper reports the findings of a study in which the nature of the association between parental smoking and respiratory disease in their children was investigated.

## Methods

The material was collected during a study of the prevalence of respiratory disease in schoolchildren and their parents in Aylesbury, Buckinghamshire, in 1971. The population consisted of all children aged 6-14 years attending seven schools in Aylesbury—a total of 2,598 children (1,328 boys and 1,270 girls). Data were collected on 2,426 children and their parents, a response rate of 93.4%.

A self-administered questionnaire was completed by the parents, who answered questions about their own and their

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children's health. The relevant questions were: (a) for each child, Does he/she usually cough during the day or at night in the winter?; (b) for each parent, (1) Do you usually bring up any phlegm from your chest first thing in the morning in winter?; (2 a) Do you smoke? If "No"; (2 b) Have you ever smoked as much as one cigarette a day for as long as a year? Parents who answered "Yes" to question (2 a) were classified as smokers. They were also asked how many cigarettes they smoked a day, how many ounces of tobacco they smoked each week, and how many cigars, large and small, they smoked each week. Those parents that answered "No" to question (2 a) and answered question (2 b) in the negative were classified as non-smokers, while those that responded in the affirmative to question (2 b) were classified as ex-smokers. The validity of the question on cough in the children when used in a self-administered questionnaire has already been established (Colley and Reid, 1970), as has that of the question on phlegm production (Krueger *et al.*, 1970).

The father was asked about his occupation and from this his social class was obtained. (*Classification of Occupation*, 1970). The number of siblings which the index child had was also recorded.

## Results

The relation in the parents between smoking habits and prevalence of phlegm was what one would have expected; prevalence rose with amount smoked. Parents were classified by smoking habit into five groups; group 1, both parents non-smokers; group 2, one parent a smoker, the other a non-smoker; group 3, both parents smokers; group 4, both parents ex-smokers or one an ex-smoker and the other a non-smoker or smoker; and group 5, one or both parents gave no data on smoking habits. Within these five groups the prevalence in the children of cough during the day or at night in the winter was determined (table I). The cough prevalence rates were lowest

in children with one or both parents ex-smokers. The gradient in prevalence over groups 1, 2, and 3 was statistically significant ( $\chi^2$  for trend 6.865;  $0.01 > P > 0.005$ ). The findings indicated an association between parental smoking habits and the prevalence of symptoms in their children.

The analysis was taken a stage further by classifying parents by both smoking habits and by their response to the question, Do you usually bring up any phlegm from your chest first thing in the morning in winter? (table II). Within each group the prevalence of cough in children was lowest among children of parents who did not report symptoms. It was highest in those children where both parents reported symptoms. Where only one parent reported the symptom the prevalence rate lay between these two extremes. Overall, there was a threefold difference in prevalence of cough between children with neither parent having the symptoms and both having the symptom.

Some of the prevalence rates in table II were based on small numbers, but the numbers in the category where neither parent had symptoms allowed a firmer conclusion. It was thus interesting to note that in this category the prevalence of cough rose from 12.4% in children of non-smoking parents to 14.3% where one parent smoked and to 14.7% where both smoked. This trend while small and not statistically significant nevertheless raised the possibility that exposure to cigarette smoke at home when parents smoked might have had some effect on the child's respiratory tract. A more precise estimate of the effects of "passive smoking" by the child was obtained by estimating the maximum daily exposure of the child to their parents' cigarette smoke. This was derived by the addition of both parents' daily cigarette consumption. Among the children of parents who did not have morning phlegm there was a small gradient for cough prevalence according to the number of cigarettes (or tobacco equivalent) smoked by the parents (table III). This gradient in prevalence is not, however, statistically significant ( $\chi^2$  trend 1.36;  $0.30 > P > 0.20$ ).

TABLE I—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits

	Parents' Smoking Group*					Total†
	1	2	3	4	5	
Percentage (No.) of children with cough	15.6 (320)	17.7 (347)	22.2 (634)	14.2 (420)	20.7 (217)	18.0 (2,338)

\*See text for composition of groups.

†Total includes 88 children for whom there were no data on cough.

TABLE II—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits and Presence of Winter Morning Phlegm

	Group 1			Group 2			Group 3			Group 4			Total*		
	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both
Winter morning phlegm in parents ..															
Percentage (No.) of children with cough ..	12.4 (274)	27.5 (40)	30.0 (5)	14.3 (420)	24.7 (97)	32.9 (17)	14.7 (369)	24.1 (159)	41.5 (69)	12.6 (499)	19.6 (98)	23.1 (13)	13.5 (1,582)	21.1 (394)	44.2 (104)

\*Total excludes 346 children for whom there were no data on cough or parents' smoking habits or morning phlegm.

TABLE III—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits, Number of Cigarettes smoked, and Presence of Winter Morning Phlegm

	Group 1		Groups 2 and 3								Group 4		Total†	
			Total No. of Cigarettes*											
			1-9		10-19		20-29		>30					
	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B
Winter morning phlegm in parents														
Percentage (No.) of children with cough .. .. .	12.4 (274)	33.3 (45)	13.3 (135)	32.1 (28)	13.8 (247)	21.9 (63)	14.9 (208)	37.6 (74)	15.9 (208)	32.7 (174)	12.6 (499)	39.8 (111)	13.56 (1,571)	24.07 (697)

N = Neither, O/B = One or both.

\*Including tobacco and cigars expressed as cigarette equivalents (see Todd, 1972).

†Total excludes 358 children for whom there were no data on cough or parents' smoking habits or morning phlegm.



Several points have to be considered in interpreting these findings. As in other studies (Holland *et al.*, 1969; Colley and Reid, 1970), social class gradients for respiratory symptoms in children were found in this series. Children with fathers in semi-skilled and unskilled occupations had higher prevalence rates for respiratory symptoms than those whose fathers were in skilled or non-manual occupations. A concentration of low social class families in the groups where both parents reported winter morning phlegm could have produced a similar pattern to that shown in table II. That this could not have accounted for the observed patterns of cough prevalence in the children may be seen in table IV, where cough prevalence is given for children in social class III according to the parents' history of phlegm production after standardization for smoking. Cough prevalence in the children increased, as before, with the presence of parental phlegm production.

TABLE IV—Prevalence in Social Class III of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm (Standardized for Parents' Smoking Habits)

Parents with winter morning phlegm	Neither	One	Both
Percentage (No.) of children with cough	15.4 (824)	27.4 (207)	32.9 (54)

Children from large families have higher prevalence rates for respiratory symptoms than those from small families (Colley, 1970), and a concentration of large families in the groups of parents with symptoms might also have resulted in the prevalence of morning cough being similar to that shown in table II. It can be seen from table V, however, that within families of similar size the same gradients for cough prevalence according to parents' phlegm production were present, indicating that differences in the number of siblings could not have explained the gradient in cough prevalence.

TABLE V—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm and Number of Siblings (Standardized for Parents' Smoking Habits)

Parents with Winter Morning Phlegm	No. of Siblings					
	Nil or 1		2		3 or More	
	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)
Neither	672	14.2	444	11.6	444	14.8
One	122	16.5	137	26.6	135	29.4
Both	25	37.9	27	37.5	52	44.6

Table excludes 348 children owing to lack of data on cough, or on parents' smoking habits or morning phlegm, or on family size.

Younger school children tend to have higher prevalence rates for winter cough than older children (Colley and Reid, 1970). If the age distributions of children in the various groups in table II had not been the same prevalence rates between these groups might also have differed, but there were no differences in age structure between these groups of children.

Conclusions drawn from the evidence in this study need to be viewed with caution because it was not possible to collect evidence which would have excluded some other interpretation of the results. It was possible, for example, that the parents' account of their own symptoms might have influenced the answers they gave for their children and that the apparent association between parents and children in their respiratory experience could have been due to parents with symptoms over-reporting symptoms in their children. The children of parents who smoked may also have been more likely to have smoked than children of non-smoking parents, and this could have resulted in an increased prevalence of cough in such children. If either of these possibilities had oc-

curred to any material extent it would have meant that, as given in table II the prevalence of cough in children from group 2 was too high in relation to cough in children from group 1 and that the prevalence of cough in children from group 3 was still higher. If the prevalence of cough in children from group 2 were to be reduced in order to correct for this and that of children from group 3 were to be corrected even more then the gradient shown in table II would probably become negative in that cough prevalence in children would have seemed to decline as more parents smoked. It therefore seems reasonable to conclude that the two possible qualifications to the data did not operate.

## Discussion

Norman-Taylor and Dickinson (1972) in their study of children's respiratory infections and parental smoking habits reported higher prevalence rates for various indices of respiratory disease among children with parents who smoke. The present study, using a single index of respiratory disease, confirms their findings. It can now be seen, however, that a direct association exists between respiratory symptoms in parents and in their children. Parental smoking has a mainly indirect effect on the child by increasing the prevalence of the parents' respiratory symptoms and thus the prevalence of respiratory symptoms in their children. The direct effect on the children's respiratory symptoms of exposure to the smoke generated when their parents smoked cigarettes seemed to be relatively small.

The reason for the association between respiratory symptoms in parent and child is not clear. The sharing of genetic susceptibility between parents and children could have led to these similarities in respiratory disease, but this is unlikely to be the whole explanation, particularly in families where both parents smoke. There is, for example, no convincing evidence that adults who take up smoking have a greater genetic susceptibility to respiratory disease than non-smokers, and therefore there is no reason to suppose that susceptibility to respiratory disease would be different in the children of smokers and non-smokers. On the other hand, smoking parents differed from the non-smokers in that they had higher prevalence rates for respiratory symptoms and the rates rose with the amount smoked, indicating some direct effect of smoking in causing their symptoms. In these circumstances the association between parents' and children's symptoms are more likely to be due to cross infection than to the sharing of genetic susceptibility.

If cross infection is indeed an important cause of respiratory symptoms in children of parents who smoke then there could well be some advantages for their children if the parents gave up the habit. In adults giving up smoking can result in a reduction in cough and expectoration and, therefore, in the chance of transmitting respiratory infections. Smoking parents, many of whom will not yet have developed severe or irreversible respiratory damage, can reasonably expect an improvement in symptoms if they give up the habit, and this would offer a promising way of reducing the risk of their children developing respiratory symptoms.

The findings in this paper need confirmation. This could be done by prevalence studies on a larger scale in other populations where, for example such aspects as the possible over-reporting of symptoms could be adequately investigated. There is a need to investigate the likely benefit to the child from parents giving up smoking. Though passive inhalation of cigarette smoke by the child has not been shown to have an important effect in this series, this aspect should nevertheless be studied in infants and preschool children, who tend to be the most susceptible to respiratory infections.

I thank Dr. J. J. A. Reid, who at the time of this study was County Medical Officer of Health, Buckinghamshire; Dr. A. W. Frigie, Aylesbury Area Medical Officer and Divisional School Medical Officer; the Buckinghamshire Education Department and the head teachers of the schools involved for their co-operation and help in this survey; Mrs. B. Hunt for the analysis of the data; Professor D. D. Reid who gave helpful advice in the preparation of this paper; and the field workers who included Mrs. B. Hunt, Miss S. J. Newby, S.R.N., Mrs. M. Pant, S.R.N., Miss J. P. E. Stocks, S.R.N., and Miss J. V. Tudhope, S.R.N.

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# Choreo-athetosis and Encephalopathy Induced by Phenytoin

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## Summary

Two patients with intractable epilepsy who had been treated with various combinations of anticonvulsant drugs developed phenytoin encephalopathy. In both patients choreo-athetoid involuntary movements were prominent. Blood phenytoin concentrations were above 30 µg/ml. When phenytoin was given in smaller doses and its level in the blood fell the involuntary movements and other clinical manifestations disappeared.

## Introduction

Nystagmus, ataxia, dizziness, and drowsiness are well-known features of phenytoin toxicity which usually occur when the blood level is greater than 20 µg/ml (Buchthal *et al.*, 1960). There have been few reports of other toxic effects on the central nervous system though Glaser (1973) pointed out that a reversible encephalopathy may occur in some patients treated with large doses of the drug. We describe two patients in whom choreo-athetoid involuntary movements were a prominent and presenting feature and in whom the involuntary movements and the encephalopathy were closely correlated with very high blood phenytoin concentrations.

## Case Reports

### CASE 1

A 31-year-old man who had attended hospital for many years for management of epilepsy was admitted for investigation of involuntary movements and intractable seizures. He had had a febrile convulsion when 2 years old and had had recurrent petit mal and major generalized seizures since he was 7. An electroencephalogram when he was aged 13 showed typical, generalized, three-per-second spike-and-wave complexes and diffuse bursts of theta and delta activity. When assessed for industrial training when aged 21 he had an I.Q. of 84 on the Wechsler Intelligence Scale. He was treated with various combinations of anticonvulsants,

including troxidone, ethosuximide, primidone, and phenytoin, but he continued to have two or three major seizures a month. When he was aged 29 Hodgkin's disease was diagnosed by biopsy of an enlarged cervical lymph node. No involvement of liver, spleen, or para-aortic nodes was seen on laparotomy and he was treated with radiotherapy to the neck. There had been no recurrence. Treatment with phenytoin 300 mg, phenobarbitone 150 mg, and ethosuximide 750 mg daily was continued. Two years later the seizures became more frequent (two to four a week) and primidone 750 mg, carbamazepine 800 mg, and phenytoin 450 mg daily were gradually substituted for the previous treatment. During the next six weeks he complained of blurred vision and ataxia, leading to frequent falls. He continued to take the drugs. The seizures continued unchanged.

On admission to hospital he was slightly drowsy but orientated. Several minor seizures were observed. He had grade I nystagmus in all directions and upward conjugate gaze was impaired. There was generalized chorea which was present at rest and was enhanced by movement, particularly by walking. Slurred and hesitant speech seemed to be due to interposed choreic movements of the lips and tongue. In the outstretched upper limbs choreiform involuntary movements were accompanied by irregular postural lapses of the fingers, which were thought to be typical of asterixis rather than chorea. The gait was unsteady, but there were no cerebellar signs in the limbs. There was no weakness or sensory impairment, the tendon reflexes were brisk, and both plantar responses were flexor. Hyperplasia of the gums was noted. The increased frequency of seizures and the encephalopathy with involuntary movements were first ascribed to a degenerative or infective disorder associated with the Hodgkin's disease. The haemoglobin, white cell count, E.S.R., liver function tests, blood urea and electrolytes, skull and chest x-ray examinations, and brain scan were normal. The background activity in the E.E.G. was fragmented and slowed and there was an excess of diffuse, irregular delta activity of moderate voltage. Generalized atypical spike-and-wave activity was prominent. The blood phenytoin concentration was 37 µg/ml.

The possibility of phenytoin encephalopathy was considered. The daily dose of phenytoin was reduced to 200 mg daily and that of primidone increased to 1 g. Carbamazepine 800 mg daily was continued. During the next six days the patient became more alert, the chorea, ataxia, and nystagmus disappeared, and the blood phenytoin level fell to 16 µg/ml. The seizures at first increased in frequency but then abated. Three weeks later he returned to work. Neurological findings at that time were normal.

### CASE 2

This 15-year-old boy was referred for management of uncontrolled epilepsy. He had had frequent minor and major seizures since the age of 2 when he had presented in status epilepticus. He had been treated with varying combinations of phenytoin, phenobarbitone, ethosuximide, and valproic acid and had been almost free

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2

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Colley, J.R.T., Holland, W.W., Corkhill, R.T. "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood" The Lancet (November 2): 1031-1034, 1974.

SUMMARY: The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest where both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis.

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# INFLUENCE OF PASSIVE SMOKING AND PARENTAL PHLEGM ON PNEUMONIA AND BRONCHITIS IN EARLY CHILDHOOD

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**Summary** The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest where both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis.

## Introduction

INFANTS who inhale the tobacco smoke generated when their parents smoke at home may have a greater risk of chest illness than the infants of non-smoking parents. We have studied the influence of parental smoking and respiratory symptoms for effects on the incidence of pneumonia and bronchitis in their children during the first five years of life.

## Methods

The data that form the basis of this paper are part of those collected during a longitudinal study of newborn infants and their families. The study was conducted in Harrow, a borough in north-west London, between 1963 and 1969 and involved all families living in six of the wards of the borough who had an infant born in the period

July 1, 1963, to June 30, 1965. A total of 2365 families had newborn infants during this period, and, of these, 2205 (93%) were included in the study. The 6.8% excluded (i.e., 160 families) had either moved away from the area before they could be visited or refused to cooperate in the study (table 1). The analysis that follows has been based upon the infants born to these families. After exclusions—for example, multiple births—2149 infants were eligible for study. Over the five years of follow-up losses inevitably occurred from the original population; these were small and are unlikely to have seriously biased the findings in the later years of follow-up. Health visitors, who received special training, administered a questionnaire to the parents, when, as part of their

TABLE 1—SURVEY POPULATION OVER THE FIVE YEARS OF FOLLOW-UP

No. of families with newborn infants born July 1, 1963, to June 30, 1965		No. of index infants at annual follow-up					
Total	Cooperated in survey	Initial visit	First	Second	Third	Fourth	Fifth
2365	2205	2149	2122	2109	2096	2097	2095

routine duties, they visited the infant and mother at home within fourteen days of the delivery. At this visit a number of items were recorded, including birth-weight in pounds to the nearest pound below.

The health visitor also administered a questionnaire which included questions on respiratory symptoms and smoking habits. In this paper positive responses to the question "Do you usually bring up any phlegm from your chest first thing in the morning in the winter?" has been used as evidence for parental respiratory disability. To elicit smoking habits the questions were: "Do you smoke?" If answered "yes", the parent was classified as a present smoker. If answered "no" the parent was asked "Have you ever smoked?" If the answer was "yes", then the parent was classified as an ex-smoker. If answered "no" the parent was asked "Have you ever smoked as much as one cigarette a day for as long as a year?" An answer "no" classified parents as non-smokers. The present smokers were also asked "How many cigarettes are you smoking now?" The validity of the answers to these questions has already been established.<sup>1</sup>

The families were followed up annually for the next five years by postal questionnaires. Each year parents were asked the following questions. For the infant, "Has he/she had in the past twelve months bronchitis? Pneumonia?" For the parents, "Did you usually bring up any phlegm from your chest first thing in the morning last winter?" Smoking habits were assessed using the question "Do you smoke?" If "yes", "How many are

you smoking now?" The validity of answers to the question on infant bronchitis and pneumonia was assessed by checking, in a sample, the parents' account of such an illness with the family doctor's case-notes. The level of agreement was adequate and corresponded to that obtained in other studies where mothers were asked about their children's past health. The validity of the question on phlegm production in the parents has also been established.<sup>2</sup>

In the tables that follow, parents have been classified according to their smoking habits. Parents who at the initial visit had never smoked, and at the first and subsequent follow-ups had not taken up the habit, were classified at each follow-up as non-smokers. In the same way parents who at the initial visit were present smokers, and at the first and subsequent follow-ups did not give up the habit, were classified on each occasion as present smokers. There remained a further group of parents who had changed their habits. These included parents who at the initial visit were ex-smokers. They had been permanently allocated, irrespective of whether or not they took up smoking again, to the "ex-smokers or changed habits" group. In addition there is a further group of parents who were either non-smokers or smokers at the initial visit but who changed their habits during their follow-up. When this occurred they were reclassified permanently as members of the "ex-smokers or changed habits" group. In this way, for example, parents who were smokers at the initial and first and second follow-up visits would be classified as such at these follow-ups. If on the third follow-up they gave up smoking they would be moved to the "ex-smoker or changed habits" group for that and subsequent follow-up years. This method of classification ensures that at each follow-up year the group of "non-smoking" and "present smoking" parents contains parents with consistent smoking habits. The diminishing numbers at each follow-up in these two groups is a result of parents changing their habits and is balanced by the increasing numbers in the "ex-smokers and changed habits" group. The totals in these tables do not correspond to those in table 1. This is accounted for by the exclusion of single-parent families and by absent data.

### Results

The annual incidence per 100 children of pneumonia and bronchitis is given in table II by parents' smoking habit. Parents have been classified into one of four groups: (1) both parents non-smokers; (2) one parent smoker, the other non-smoker; (3) both parents smokers; (4) both parents ex-smokers, or one an ex-smoker, or parents who changed their smoking habits during the study. The incidence of pneumonia and

TABLE II—PNEUMONIA AND BRONCHITIS BY PARENTS' SMOKING HABITS

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis				
	Both non-smokers	One smoker	Both smokers	Both ex-smokers or one ex-smoker or smoking habit changed	All
1	7.8 (372)	11.4 (552)	17.6 (478)	9.2 (675)	11.5 (2077)
2	8.1 (358)	9.3 (444)	8.9 (438)	7.4 (758)	8.3 (2048)
3	7.0 (342)	10.2 (460)	9.1 (396)	8.9 (834)	8.9 (2032)
4	8.4 (323)	8.3 (408)	9.0 (357)	8.4 (882)	8.5 (1970)
5	7.5 (319)	6.7 (374)	6.5 (340)	6.4 (754)	6.7 (1899)

bronchitis in the infant shows a gradient by parents' smoking habit in the first year of life. Incidence is lowest in infants with both parents non-smokers, highest where both parents smoke, and lies between these values where one parent smokes. This is a statistically significant gradient ( $p < 0.0005$ ). In subsequent years there is no such clear gradient.

In table III parents have been classified both by their smoking habits and by their response to the question "Did you usually bring up any phlegm from your chest first thing in the morning in the last winter?" In all categories except one, the incidence within a smoking category is higher among children where one or both parents have winter morning phlegm than in children whose parents are both free of this symptom. Some of the incidence-rates in the children—in particular those whose parents are both non-smokers and who have winter morning phlegm—are based upon small numbers and therefore may not be wholly reliable. On the other hand, the incidence-rates in children where neither parent has symptoms, whether they smoke or not, are based upon substantial numbers. In them in the first year of life a consistent gradient is seen in the incidence of pneumonia and bronchitis in the children in relation to the parents' smoking habits. The rates are lowest in children of non-smoking parents and highest where

TABLE III—PNEUMONIA AND BRONCHITIS IN THE FIRST FIVE YEARS OF LIFE BY PARENTS' SMOKING HABIT AND MORNING PHEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
1	7.4 (343)	10.3 (29)	10.4 (424)	14.8 (128)	15.3 (339)	23.0 (139)	8.2 (546)	13.2 (129)	10.1 (1652)	16.7 (425)
2	8.1 (322)	8.3 (36)	7.1 (365)	15.5 (129)	8.7 (286)	9.2 (152)	6.5 (399)	10.7 (159)	7.4 (1572)	11.3 (476)
3	6.9 (305)	8.1 (37)	10.5 (353)	9.4 (107)	7.9 (342)	11.0 (134)	8.2 (641)	11.6 (173)	8.4 (1561)	10.6 (471)
4	8.0 (287)	11.1 (36)	7.5 (306)	10.8 (102)	7.6 (236)	11.6 (121)	8.2 (695)	9.1 (187)	7.9 (1524)	10.3 (446)
5	6.7 (285)	14.7 (34)	5.4 (267)	9.4 (107)	3.9 (208)	10.6 (132)	6.4 (737)	7.3 (219)	5.9 (1497)	9.1 (492)

N = neither with winter morning phlegm. O/S = one or both with winter morning phlegm.

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TABLE IV—PNEUMONIA AND BRONCHITIS BY NUMBER OF CIGARETTES SMOKED PER DAY BY PARENTS AND WINTER MORNING PHLEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One or both smokers* of following number of cigarettes per day†:							
			1-14		15-24		25 and over			
	N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
1	7.6 (343)	10.3 (29)	10.4 (269)	15.1 (53)	11.1 (171)	14.5 (76)	15.2 (323)	23.2 (138)		
2	8.1 (322)	8.3 (36)	5.2 (231)	16.4 (55)	8.6 (151)	14.5 (62)	9.7 (269)	9.8 (164)		
3	6.9 (305)	8.1 (37)	11.2 (206)	8.6 (58)	8.2 (146)	9.5 (42)	8.6 (243)	11.2 (161)		
4	8.0 (287)	11.1 (36)	5.5 (163)	13.3 (45)	7.4 (136)	11.5 (52)	9.1 (243)	10.3 (126)		
5	6.7 (285)	14.7 (34)	6.3 (144)	11.4 (44)	4.4 (113)	7.6 (53)	4.1 (218)	10.6 (142)		

\* Excluding parent pairs where one or both are ex-smokers or changed smoking habit.

† Includes tobacco and cigars expressed as cigarette equivalents (see Todd<sup>19</sup>).

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

both parents smoke. In children over the age of a year there is, however, no consistent gradient.

Exposure of the child to cigarette smoke may be more precisely estimated from the total daily cigarette consumption of both parents. In table IV the incidence of pneumonia and bronchitis is given for parent pairs smoking between them 1-14, 15-24, and 25 or more cigarettes per day, by the presence of winter morning phlegm. A clear gradient of increasing incidence is seen in the first year of life that is independent of the presence of winter morning phlegm and is of the same size as that in table III. In the second year and thereafter the pattern is not consistent and thus does not suggest an effect of exposure to tobacco smoke at ages over one year.

The gradients of incidence, particularly those attributable to passive smoking in the first year of life, could result from other factors which are known to influence respiratory disease in infancy—for example, social class and family size. These factors might account for the gradients if children of low social class or of large family size were concentrated in families where the parents smoked or had chest symptoms. That these factors did not explain the observed gradient can be seen in tables V and VI. In table V, the findings for social class III alone are

examined. The patterns for pneumonia and bronchitis for all children in the first year of life persist. Similarly, in table VI, where the data are subdivided by the number of siblings in the family, the patterns for pneumonia and bronchitis persist within families of the same size. This makes it unlikely that either social class or family size can be responsible for these patterns of respiratory-disease incidence.

The infants of mothers who smoke in pregnancy are, on average, lighter than those of mothers who do not smoke.<sup>3</sup> As infants of low birth-weight are more likely to suffer respiratory illness than normal-weight infants, it is possible that the gradients in respiratory disease observed in the first year of life, and in particular the effects of passive smoking, may be due, indirectly, to maternal smoking during pregnancy. In this study, birth-weight, as expected, shows a

TABLE V—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY PARENTS' SMOKING HABIT AND WINTER MORNING PHLEGM FOR SOCIAL CLASS III

Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker		All	
N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
5.9 (171)	20.0 (15)	9.5 (263)	16.5 (79)	17.1 (217)	23.9 (88)	7.1 (294)	12.1 (66)	9.8 (945)	18.2 (248)

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

gradient by parents' initial smoking habit, and to a lesser extent by winter morning phlegm. Thus parents who smoke have lighter infants than parents who do not smoke. The gradients in the incidence of pneumonia and bronchitis with parental smoking, and with winter morning phlegm, might therefore be partly attributable to differences in birth-weight. However, within different birth-weight categories the gradients for pneumonia and bronchitis with parents' smoking habits persist. Thus differences in birth-weight cannot account for the higher risk of pneumonia and bronchitis in the first year of life in children exposed to the cigarette smoke generated when their parents smoke at home.

### Discussion

An association between the respiratory symptoms

TABLE VI—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY NUMBER OF SIBLINGS AND BY PARENTS' SMOKING HABIT AND WINTER MORNING PHLEGM

No. of siblings	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
0	3.9 (153)	14.3 (14)	5.1 (177)	6.3 (32)	13.3 (165)	12.7 (55)	5.8 (258)	6.4 (47)	6.9 (753)	9.5 (148)
1	8.1 (124)	8 (7)	15.0 (146)	12.0 (50)	13.6 (103)	34.1 (44)	9.6 (178)	17.5 (40)	10.9 (551)	19.9 (141)
2 and more	15.2 (66)	12.5 (8)	15.8 (101)	23.4 (46)	22.5 (71)	25.0 (40)	11.8 (110)	16.7 (42)	15.8 (348)	21.3 (136)

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

in parents and in their school-age children was reported by Colley.<sup>4</sup> The present study demonstrates that this association is also found in younger children as early as the first year of life. The nature of this association, as Colley noted, is not clear. He concluded that it was unlikely to be an artefact due, for example, to parents with symptoms over-reporting symptoms in their children. In the present study a sample of parents had their account of respiratory illnesses in their children checked against the doctors' records. The close agreement between these two accounts makes it unlikely that over-reporting in families where parents have symptoms has occurred to any important extent.

The association could be a result of shared genetic susceptibility to respiratory disease between parents and children, to living in the same home environment, and to cross-infection within the family. Twin studies in adults have not been notably successful in assessing the genetic contribution to adult chronic respiratory disease, and no studies have yet been reported where this aspect was investigated in parents and their children. The contribution made by the other factors to this association can, at present, only be guessed at.

Passive smoking by the infant, after differences in birth-weight and parental respiratory symptoms have been allowed for, increases the risk to the infant of pneumonia and bronchitis in the first year of life. When both parents smoke, this risk is almost double that of infants with non-smoking parents. The findings confirm and extend those of Harlap and Davies.<sup>5</sup> These workers did not, however, have information on fathers' smoking habits, nor did they take account of parents' respiratory symptoms.

A picture has thus emerged of a serious risk to infants in the first year of life from exposure to their parents' cigarette smoke. In contrast, between one and five years of age, there does not appear to be any important effect of passive smoking in increasing the risk of pneumonia and bronchitis. Colley,<sup>4</sup> in 6-14-year-olds also found no association between passive smoking and the prevalence of chronic cough.

The estimates of children's exposure to cigarette smoke in this study are crude, being based either on whether parents were smokers or not, or on their total daily cigarette consumption. The smoke exposure of the children may have been overestimated, since parents—in particular the father—will smoke outside the home, or at times when the infant is not present. The effects on the child may thus have resulted from exposure to levels of cigarette smoke less than those suggested by our study.

The evidence from this study, taken with that of Harlap and Davies,<sup>5</sup> provides convincing reasons for warning parents who smoke of the risks this entails for their children both from the direct effect of their cigarette smoke and from the presence of their respiratory symptoms. Attacks of pneumonia and bronchitis, particularly in the first year of life, can still result in infant death despite prompt and vigorous treatment. In those that survive such illnesses and recover clinically, the evidence points to some damage to the respiratory tract as indicated by an increased prevalence of chest symptoms and deficits in ventilatory function found in later childhood.<sup>4</sup> The

longer-term consequences of such childhood illnesses have been underlined by the findings in a cohort of infants followed to the age of 20.<sup>6</sup> At this age the prevalence of chronic cough, after allowing for current smoking habits, social class of father, and air-pollution exposure, was higher in those with a documented history of a chest illness under the age of 2 years than in those without this history. If, by the age of 20, such long-term effects are found, these could persist into middle and late adult life and contribute to the evolution of chronic respiratory disease.

Opportunities for the prevention of serious respiratory disease in infancy and childhood are few. If parents who smoke give up the habit they can reasonably expect to lose, or at least experience an improvement in, their respiratory symptoms. This might well result in reduction of respiratory illnesses in their children. At the same time the absence of cigarette smoke in the home could be expected to diminish the risk of attacks of pneumonia and bronchitis in their children during the first year of life.

This study was conducted jointly with the Health, Welfare, and Children's Department of the London Borough of Harrow, and we would particularly like to thank the Superintendent Health Visitors and their staff, the Senior Administrative Assistant in the Personnel Health Section and his staff, and others who took part for their help and cooperation in this study. Our thanks go to the fieldworkers from the Department of Community Medicine for the maintenance of the records and for their diligence in carrying out the fieldwork during the five years of follow-up. We are also grateful to the statistical assistants of the department for carrying out the analysis of the data.

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"The atomic physicists were as clever, as modest, as self-seeking, as mean, as argumentative and just as concerned for humanity as the microbe hunters. The physicists worked to produce a weapon of war, but there is no real evidence that the nationalistic arguments which convinced them that their efforts were right and just were any different from those that so affected Koch and Pasteur half a century earlier; and the intellectual challenge was just as great, and grappling with it just as enjoyable. . . . The physicists' work was widely seen as being culpable because it was applied to the taking of life; the first two atomic bombs did so on a vast and horrifying scale. But it was Pasteur, and not some atomic physicist, who in 1870 said of the Germans, 'I want to see the war prolonged into the depths of winter, so that all those vandals confronting us shall perish of cold and hunger and disease.'"—ROBERT REID, *Microbes and Men*; p. 168. London: B.B.C. Publications. 1974. £2.50.

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Holma, B., Winding, O. "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen" Archives of Environmental Health (March/April): 86-93, 1977.

ABSTRACT. The effect of 109 social, medical, housing, and hygienic factors on morbidity of 2,096 individuals was studied in 881 apartments in Copenhagen. "Thriving" (satisfaction), followed by "housing standard" and "personal hygiene," turned out to be the most prominent predictor for health. "Thriving of parents" was also important for the health of children. Excluding "thriving" in the analyses, "housing standard" and "personal hygiene" or components of these group factors were the important predictors for the health of the population studied, except for children below 3 years of age. For the health of these, the number of rooms used for sleeping purposes was the best predictor. The only other parameter found to influence the morbidities investigated was the total yearly income of the family, which was found to be a secondary predictor for adult morbidity during the last month of the investigation (March 1973). The analyses applied were Pearson correlation, AID-program, factor and multiple regression analyses.

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# Housing, Hygiene, and Health

## A Study in Old Residential Areas in Copenhagen

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### ABSTRACT

The effect of 109 social, medical, housing, and hygienic factors on morbidity of 2,096 individuals was studied in 881 apartments in Copenhagen. "Thriving" (satisfaction), followed by "housing standard" and "personal hygiene," turned out to be the most prominent predictor for health. "Thriving of parents" was also important for the health of children. Excluding "thriving" in the analyses, "housing standard" and "personal hygiene" or components of these group factors were the important predictors for the health of the population studied, except for children below 3 years of age. For the health of these, the number of rooms used for sleeping purposes was the best predictor. The only other parameter found to influence the morbidities investigated was the total yearly income of the family, which was found to be a secondary predictor for adult morbidity during the last month of the investigation (March 1973). The analyses applied were Pearson correlation, AID-program, factor and multiple regression analyses.

STUDIES HAVE revealed that factors such as overcrowding, lack of basic sanitation (e.g., cold or hot water supply), garbage accumulation, and poor construction with leaky roofs or cracked walls exert substantial influence on health. However, extreme conditions are seldom found in developed countries, and the relative importance of various factors in housing conditions is difficult to analyze. Thus, contradictory or negative results have been obtained in the developed countries with respect to the relative importance of overcrowding, socioeconomic conditions, occupation, education, housing conditions, rehousing, etc., as they may affect morbidity.<sup>1</sup>

During childhood, the area of residence, parents' social level, family size, history of respiratory diseases, and impairment of ventilatory function of the lungs influence health in adult life.<sup>2-4</sup> A survey covering the field of housing and health was made by A.E. Martin<sup>5</sup> in the United Kingdom, and by V. Christensen<sup>6</sup> in Scandinavia.

### Method

Six residential areas of Copenhagen were studied. Within each area we sampled a cluster of successive house numbers and stories. We included an equal number of men and women. The districts under study represented older houses in the central part of Copenhagen.

District One (Oesterbro) is characterized by wide streets with trees and small parks. Buildings are mainly large, fashionable-looking, older apartment houses containing large well-lighted flats with up to ten rooms or more, some with a desirable view. In this area, 183 families were questioned (89 males and 94 females).

District Two similarly consists of large, well-kept apartment houses with an exclusive location by one of the artificial lakes of Copenhagen (Sortedsøen). The flats are large and sunny, but about 100 m from the lake the

area borders on one of the most closely built-up and densely populated areas in Copenhagen (District Five), resulting in an inevitable interaction between the extremes of the social classes, especially as far as children are concerned. In this area, 91 families were questioned (33 males and 58 females).

District Three, nicknamed "Potatorows," is on the opposite side of the same lake. The buildings are low, well-separated, single-family houses about 100 years of age. Each house contains up to three small flats. The original quality of the houses was poor (small and damp, without shower, bath tub, or hot water installations). In front of the houses are small, well-kept gardens, and the friendly surroundings have attracted new social groups to the area. Simultaneously, extensive interior modernization has taken place, especially concerning hygienic facilities. In this area, 199 families were questioned (71 males and 128 females).

District Four is situated in a closed area between a main road (Oesterbrogade) and a big park. The houses were built in the midnineteenth century, after a cholera epidemic, as dwellings for workers. They are four long, two-story buildings divided into two-storied flats with separate house numbers. The flats are very small, usually not more than 25 m<sup>2</sup>, and without hygienic or sanitary installations. The area includes an assembly building and common houses for bathing and washing. For each group of ten flats there is a chemical lavatory in a small addition to the houses. In front of each flat is a small garden, 10-20 m<sup>2</sup>. In spite of the smallness of the flats and their very limited facilities, the inhabitants find so many compensating qualities in the surroundings that they express general contentment. In this area, 43 families were questioned (22 males and 21 females).

District Five (Ryesgade) is situated alongside District Two, less than 100 m away. It is one of the most popu-

lous streets in Copenhagen, and had a population of 70,000 people before partial demolition began in the area. The buildings are five- and six-story apartment houses with up to three back buildings. An ordinary complex will consist of a front building and two back buildings. The flats are small and insufficiently furnished with hygienic facilities. Heating is mainly separate for each room and is dependent on oil stoves or the like. Daylight in the flats is scanty, and recreation facilities for children and grown-ups are nonexistent in the district. In this area, 214 families have been questioned (101 males and 113 females).

District Six is situated in the inner city (Noerrebro) and has the nickname "the black square." The buildings in the area must be described as slums and are partly condemned. Quality of flats is comparable with that in District Five, but the area is generally considered the worst of the districts studied. Typical flats in districts Five and Six have two rooms and awkward entrance facilities. Narcotics are said to be a problem in this district. In this area, 135 families were questioned (63 males and 72 females).

The respondent was asked to fill out a questionnaire of 109 questions with alternate and/or grouped answers. Instruction was given by the interviewers (medical students), who returned 1½ hours later to collect the forms after having given supplementary instructions, as necessary. Up to five repeated attempts were made to contact persons who were not available or did not answer. The interviewers received their instructions partly as a group at an evening course and partly individually before visiting the districts.

Univariate tables were made for all variables. From a Pearson correlation matrix a screening selected all significant correlations. Corresponding bivariate tables were made in order to study the correlations more closely.

Morbidity, the dependent variable, was defined as the number of episodes of illness, regardless of the duration. All other answers were considered independent variables. We used an Automatic Interaction Detector (AID) program to split the material into groups of respondents characterized by discrete values of one or more (uncorrelated) predictors. The principle for the split is a successive search for the predictor that gives the maximum difference between sums of squares for the dependent variable in the two groups. In this paper, the AID results are illustrated as figures forming "three-structures" of "original" and "split" groups.

## Results

### Frequency Tables

From 930 initial questionnaires the number of cases obtained was 881, covering 2,096 individuals—a response rate of 94.7%. The sample amounted to 12% of the total population in the areas examined; i.e., in District One, 10.5%; in District Two, 19.0%; in District Three, 10.5%; in District Four, 5.5%; in District Five, 12.0%; and in District Six, 17.0% of the population based on the statistical yearbook for Copenhagen 1973.<sup>7</sup>

A two-way display of age and sex in the population investigated is shown in Figure 1. Other characteristics of the different areas are given in Tables 1 and 2. From Table 1 it can be seen that the smallest dwellings (< 25 m<sup>2</sup>) are most frequent (64.8%) in District Four and the largest ones (> 200 m<sup>2</sup>) are to be found in District One and Two.

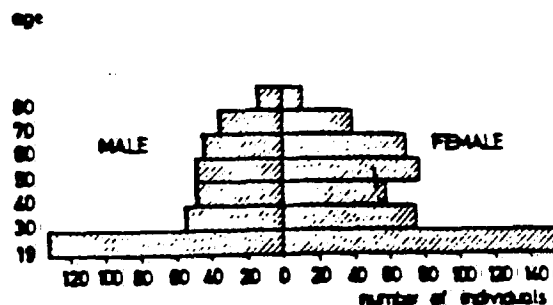


Fig. 1. Respondents' distribution by age and sex.

A low standard of housing is found in Districts Four, Five, and Six, characterized by, among other things, drafts and cold and a lack of hot water or bath tub, especially in District Four, where bathing facilities do not exist. Also in District Four, water closets outside the dwellings are found in up to 90.5% of the cases. However, in this district most people are content with their area of residence and present excellent personal hygiene as compared with the other districts (Table 1).

The highest average figure for overcrowding, measured as individuals per room (kitchen included), was 0.68 in District Five (Table 2). The best housing standards are found in Districts One and Two, while Four, Five, and Six are inferior in this respect.

A summarized description of morbidity in the different areas is found in Table 3. On the whole, morbidity was low in District Two and high in District Five for all age groups, the 3- to 6-year-old children being an exception, with higher morbidity in District Three.

The highest morbidities were reported from District Five, which has the lowest housing standard next to that of District Four. In this latter district the morbidity of the adults was high, but the effect of environment and other factors on child morbidity could not be evaluated on account of the unusually small number of children living in this district.

The lowest morbidity was found in District Two. This district was rather homogeneous and did not show the large variation in housing standards found in other districts.

In District Five and especially in District Six the "thriving" was lowest. Almost every second person expressed on absolute intention of changing to another dwelling and district. However, in the other districts that represented old houses of low standards, nobody expressed any great wish or intention to move. Those who wished to move from District Four, for instance, represented only 7% and 4.8% of the population, with complaints about dwelling and area of residence, respectively. The people in this district have given public expression to their desire to preserve the area in its present condition, contrary to the authorities' intention to clear the area because of the low hygienic standard of the buildings.

### Correlation Matrix

From the correlation matrix some associations between morbidity and other examined variables may be suggested. For 1- to 6-year-old children in these areas of Copen-

Table 1.—Some Characteristics of the Six Residential Districts in Copenhagen

CHARACTERISTICS	"ONE" N %	"TWO" N %	"THREE" N %	"FOUR" N %	"FIVE" N %	"SIX" N %
Dwelling < 25 sq.m.	0 0.0	4 4.5	17 9.2	27 64.3	18 8.5	19 14.4
Dwelling > 100 sq.m.	76 43.7	44 49.4	28 15.2	1 2.4	24 11.4	15 11.4
Dwelling > 200 sq.m.	23 13.2	5 5.6	2 1.1	0 0.0	0 0.0	0 0.0
Dwelling > 6 rooms	28 15.2	14 15.2	17 8.5	0 0.0	8 3.6	9 6.6
Draft and cold	8 4.3	7 7.7	14 7.0	4 9.1	46 21.1	32 23.5
Hot water lacking	8 4.3	6 6.7	31 16.2	29 78.4	114 54.8	61 46.9
Shower lacking	22 11.9	17 19.5	90 47.1	36 100.0	175 83.3	108 35.7
Bath tub lacking	38 20.5	22 26.5	129 69.4	36 100.0	196 95.1	118 95.9
Single room heating	25 14.0	6 6.7	46 24.7	26 65.0	106 53.0	50 39.4
Closet outside dwell.	4 2.2	6 6.7	17 8.6	38 90.5	35 16.1	24 18.0
Danger of accidents in dwelling	14 7.7	7 7.7	31 15.7	9 21.4	63 29.0	43 32.1
Contentment with dwelling	65 35.1	48 52.2	83 41.3	14 31.8	27 12.3	17 12.5
Contentment with "district"	77 41.6	43 46.7	105 52.2	36 83.7	27 12.3	14 10.3
Occup.: Workers	17 9.5	2 2.2	18 9.2	8 19.0	69 32.2	46 34.3
Absolutely intent on changing dwelling	34 18.5	12 13.2	36 18.2	3 7.1	106 47.9	74 55.2
Income > 100,000 d.kr. per year	40 23.1	16 18.2	16 8.4	0 0.0	6 3.0	2 1.5
Education level high	44 24.4	24 26.7	73 36.5	15 35.7	19 9.7	22 16.3
Education level low	57 31.7	32 35.6	75 37.6	18 42.9	153 72.1	96 71.1
Never using shower	32 18.2	13 15.7	39 19.8	3 7.0	48 22.9	17 13.3
Never using bath tub	45 24.7	28 33.7	108 55.4	23 56.1	139 68.5	86 68.8
> 10 cigarettes per day	33 27.3	19 38.8	32 28.3	16 48.5	55 37.7	39 40.2

N = Number of respondents  
% = Percentage of respondents within the district

hagen, reported morbidity in the period March 1972-March 1973 was correlated with the parents' dissatisfaction with their partner's occupation ( $P < .01$ ), the number of small children in the family ( $P < .01$ ), the parents' dissatisfaction with the environment and spare-time facilities within

the area of residence ( $P < .05$ ) and with their housing standard ( $P < .05$ ), as well as with parents' morbidity ( $P < .05$ ), and common colds in particular ( $P < .01$ ). For the 7-18 year age group, morbidity was correlated with the morbidity of the parents ( $P < .01$ ), especially in regard to the parents'

Table 2.—Population Characteristics of the Six Residential Districts in Copenhagen

Characteristics	ONE		TWO		THREE		FOUR		FIVE		SIX	
	N	%	N	%	N	%	N	%	N	%	N	%
Men responding	89	48.6	33	36.3	71	35.7	22	51.2	101	47.2	63	46.7
Women responding	94	51.4	58	63.7	128	64.3	21	48.8	113	52.8	72	53.3
Children 7-18	58		47		42		0		76		41	
Children 3-6	27		12		26		1		26		25	
Children 1 & 2	25		16		18		3		31		23	
Other family members	172		115		149		15		177		111	
Individuals	460		281		434		62		524		335	
Individuals per room kitchen incl.		0.48		0.52		0.52		0.58		0.68		0.66

N= Number of respondents

%= Percentage of respondents within the district

Table 3.—Self-Reported Morbidity of More Than One Day During the Last 12 Months in Different Age Groups within the Districts

Characteristics	ONE		TWO		THREE		FOUR		FIVE		SIX	
	N	%	N	%	N	%	N	%	N	%	N	%
Adult	94	53.4	43	47.3	109	56.5	26	65.0	151	69.9	84	63.6
Children 7-18	58	63.0	47	43.3	42	62.5	0	0	76	76.4	41	64.3
Children 3-6	22	60.0	12	44.4	26	76.0	2	50.0	26	64.5	25	56.5
Children 1 & 2	25	68.0	16	65.0	18	77.3	3	60.0	31	78.4	23	75.9

N= Number of respondents

%= Percentage of respondents within the age group in the district

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respiratory diseases ( $P < .05$ ).

Morbidity of adults was correlated with dissatisfaction with their partner's occupation ( $P < .01$ ), the quality of housing ( $P < .01$ ), and with dissatisfaction with the environment in the district, i.e., the standard of the district in relation to the other districts ( $P < .05$ ). Respiratory symptoms in particular seemed to be responsible for their morbidity, expressed as coughing, phlegm production, and wheezing in the chest. Illnesses of the adults during the last month of study (March 1973) were also related to these respiratory symptoms ( $P < .05$ ) and coincided with an increased morbidity among the children ( $P < .05$ ).

In addition to the cited results, a great number of correlations that did not concern morbidity were found. None of these was surprising.

#### AID Analysis of Single Predictors

Analysis of morbidity of adults within the last 12 months showed a split into seven groups (Fig. 2). Fatiguing work at home formed the basis for the primary split. The group with outspoken complaint of fatiguing work and with higher morbidity showed a secondary split into a still higher morbidity level in the socially worse districts, namely, Districts Five and Six, and a lower morbidity for those living in Districts One, Two, Three, and Four. For the other group with little or no fatiguing work at home, the secondary split was based on the predictor "contentment with the dwelling." Those not content with their dwelling were further split by the predictor "drafts and cold," and those satisfied with their dwelling were split once more by "fatiguing work at home." Contentment with one's occupation caused a further split within this last group.

The corresponding morbidity of adults within the last month (March 1973) showed a primary split based on the

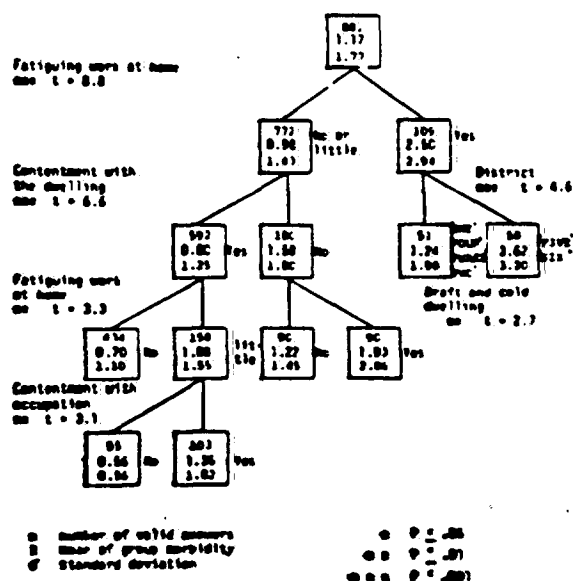


Fig. 2. Morbidity of adults during 12 months: AID analysis of single predictors.

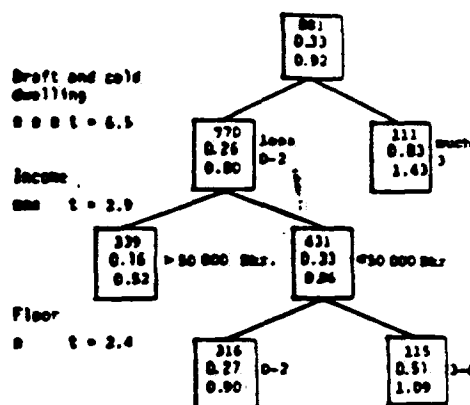


Fig. 3. Morbidity of adults during last month: AID analysis of single predictors. For key to Figures and symbols, see Figure 2.

housing standard, expressed as drafts and cold in the dwelling, while the yearly income of the family became a secondary predictor for those complaining less about drafts and cold in the dwellings (Fig. 3). For those with a higher income, the level of the apartment above the street was a third predictor for their morbidity.

In a separate analysis of the 228 single individuals included in the study, it was found that the morbidity during the last year was predicted by fatiguing work at home. For those not stressed by this factor, morbidity was predicted by districts (Fig. 4). The morbidity of the 653 married persons was primarily predicted by their contentment with their dwellings. Complainers who had a higher morbidity were further split by the presence or absence of dampness in the dwelling, and of these, those without

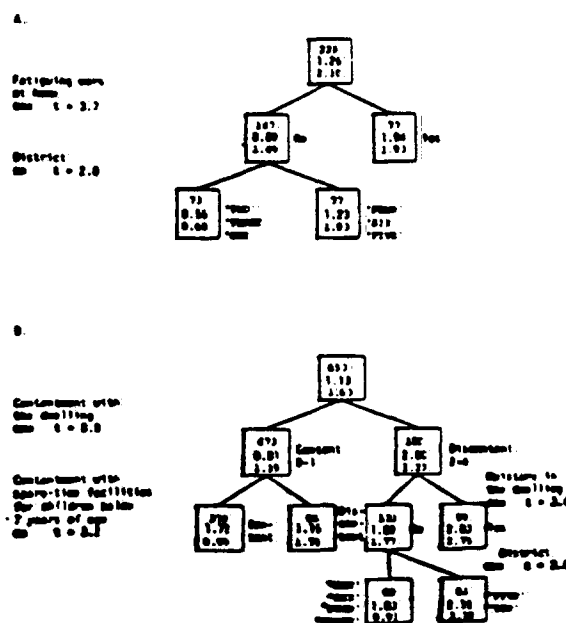


Fig. 4. Morbidity of single persons (A) and married persons (B). AID analysis of single predictors. For key to Figures and symbols, see Figure 2.

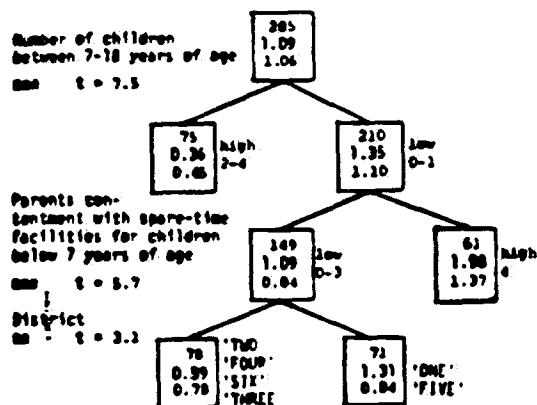


Fig. 5. Morbidity of children of 1-18 years of age: AID analysis of single-predictors. For key to Figures and symbols, see Figure 2.

dampness had a lower morbidity and showed a tertiary split by district. Morbidity for the group with high contentment with their dwelling in the primary split was in the next step predicted by their contentment with spare-time facilities for children under 7 years of age. Those content with the facilities had a lower morbidity (Fig. 4).

The mean morbidity of all children studied was increased in families with few children in the age group 7-18 years of age. The secondary predictor was their parents' contentment with the spare-time facilities for the children under 7 years of age. Children of parents who were least content with these facilities had the highest morbidity.

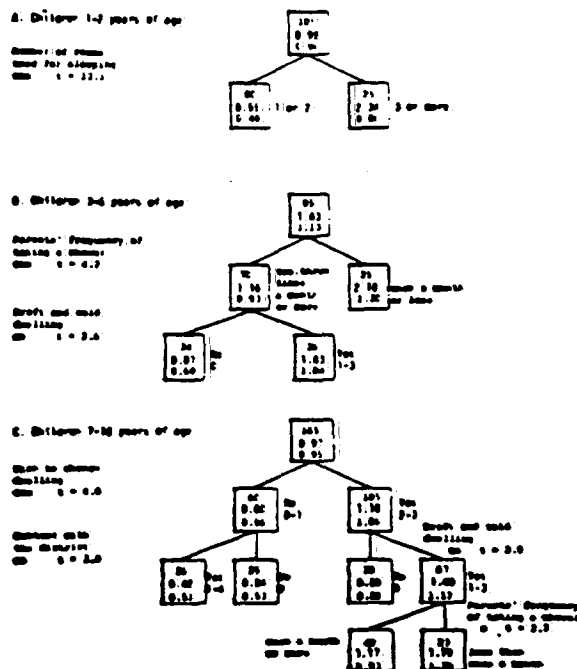


Fig. 6. Morbidity of children 1-2 years of age (A), 3-6 years of age (B), and 7-18 years of age (C). AID analysis of single-predictors. For key to Figures and symbols, see Figure 2.

A third predictor for morbidity was the area of residence (Fig. 5).

The morbidity of the youngest children investigated, 1 and 2 years of age, was predicted by the number of rooms used for sleeping purposes at home (Fig. 6). The best predictor for the morbidity of children 3-6 years of age was the personal hygiene of their parents, measured as the frequency of taking showers (Fig. 6). Thus, parents taking a shower with a frequency of less than once a month were associated with an increased morbidity of this age group of children. For families with better hygiene in this respect, the housing standard, expressed as drafts and cold in the dwelling, became another predictor for the morbidity of these children.

The morbidity of children 7-18 years of age (Fig. 6) was in the first place predicted by the parents' strong wish to change their dwelling, and in the second place by the discomfort from drafts and cold. The third predictor was the parents' personal hygiene, i.e., their frequency of taking a shower. The group with low morbidity in the first step was further split by the parents' contentment with the area of residence.

#### AID Analysis of Grouped Predictors

After the split of the material into homogeneous morbidity groups on the basis of single predictors, we combined predictors into group factors: "thriving," "housing standard," "personal hygiene," "tobacco consumption," and "alcohol consumption." The specific procedures may be obtained from the authors.

"Thriving" refers to the level of contentment as studied by the following parameters: respondent and partner's contentment with dwelling, district, neighbors, and occupation; their desire to move or to change place of

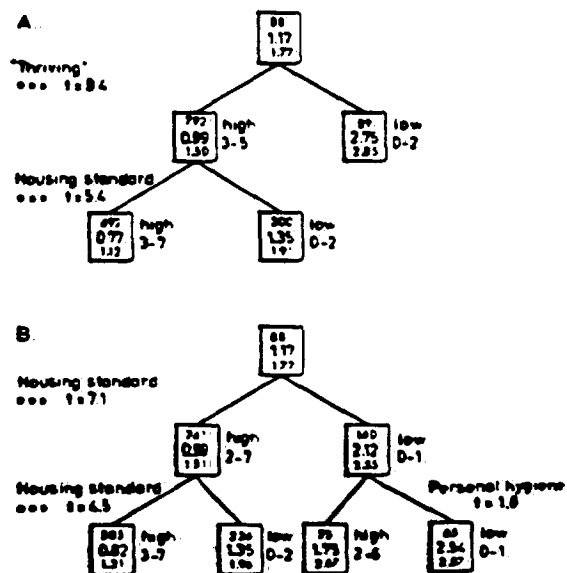


Fig. 7. Morbidity of adults. "Thriving" factor included (A) and excluded (B) in the AID analysis of grouped predictors. For key to Figures and symbols, see Figure 2.



occupation; and the respondent's contentment with spare-time facilities for children 3-6 and 7-18 years old. The "thriving" factor eliminated the other group factors, with the exception of "housing standard," as a predictor for splitting into groups by morbidity during the last year (Fig. 7). As thriving may be questionable as an independent variable, analysis was also undertaken with this factor excluded. Such an analysis yielded "housing standard" as the best predictor for adult morbidity, followed by "personal hygiene" (Fig. 7).

In analyses in which the adults' cases of illness, inclusive of chronic symptoms, were analyzed in an analogous way, "thriving" turned out to be the best predictor, followed by "housing standard" for the high "thriving" and "personal hygiene" for the low "thriving." With better hygiene, "thriving" again became the dominant predictor for those in the low "thriving" group, while "housing standard" was more important for those in the group with high "thriving." In a corresponding analysis where "thriving" was excluded, only "housing standard" remained as a predictor for morbidity.

The morbidity of adults during the last month (March 1973) was best predicted by their "thriving," followed by "housing standard" for those with high "thriving." Exclusion of "thriving" from the analysis yielded "housing standard" as the only predictor for morbidity.

An investigation of the unmarried persons by the AID analysis of grouped factors showed that "personal hygiene" was the only predictor for their morbidity during the last year (March 1972-March 1973); this was true whether the "thriving" factor was included or not. On the other hand, as far as the married respondents were concerned, the AID analysis showed that the "thriving" factor was the dominating predictor for their morbidity during the year of the investigation. For persons with low "thriving" and high morbidity no other predictors turned up. The morbidity of persons with high "thriving" and better health was further predicted by "housing standard," again followed by "thriving." In a corresponding analysis, where the "thriving" factor was excluded, "housing standard" turned out to be the prominent predictor for morbidity of married respondents.

When the respondent units, i.e., the respondents including any other family members, are considered as a target group, and the morbidity of the mean individual in these units is sought, the corresponding AID analysis shows that the predictor "thriving" again occurred as the dominant factor, followed by "housing standard." In a further analysis, when the predictor "thriving" was excluded, "housing standard" once more turned out as the only predictor for morbidity.

#### *Multiple Regression Analysis*

An attempt to use step-wise multiple regression technique (twenty-nine of the fifty-seven most significant variables) to obtain more quantitative evaluations gave as "best" result for the morbidity an explanation of 35% of the total variance, and this was only true for the 7- to 18-year-old children. The corresponding analysis with the variables grouped into factors of "housing standard," "personal hygiene," "alcohol consumption," "tobacco con-

sumption," and "thriving" did not yield more conclusive results.

#### *Discussion*

A comparison between our results and earlier studies in which housing standard and related factors have been investigated, e.g., Vagn Christensen's study in 1956,<sup>6</sup> is difficult, primarily because of the lack of objective measures of the "hygienic standard" used in these studies. Christensen used mortality among children of 0-2 years of age as an indication of low housing standard. Furthermore, our results from 1973 are not comparable with these studies because of the changes which have occurred since then in, for example, the social structure and the standard of living.

On the other hand, many epidemiological studies have not given attention to whether the study's relationships were linear or followed an irregular, logarithmic, or other function. For linear relationships correlation analysis might be sufficient, but for, e.g., irregular relationships such as those for quality of life, the nonlinear dependent AID analysis gives more valuable information. This was one of the reasons we used this form of analysis in our study.

In this study, which is concerned with morbidity in general, the factor "thriving" (satisfaction) was the most prominent predictor for health as compared with other group factors, such as "housing standard," "personal hygiene," "tobacco consumption," and "alcohol consumption." Like morbidity, however, thriving can to a great extent be considered as a function of the society. Thus thriving and morbidity have many connections in common and do not necessarily express a direct connection of causes, even though it is well known that thriving influences our well-being and thereby our health. An interesting aspect of this investigation, however, was that the connection between thriving and morbidity was stronger than the correlation between morbidity and other hygienic and social factors. Furthermore, the most outstanding correlation coefficient found in this study concerned the morbidity of children under 7 years of age and the parents' dissatisfaction with the spare-time facilities for this age group, and, further, the parents' dissatisfaction with their partner's occupation (two of the thirteen components in the group factor "thriving").

That thriving turned out to be the most prominent factor for morbidity in general was surprising, but not many studies have been performed in which the relative importance of this factor is analyzed in comparison with others. However, in 1974 Kato et al.,<sup>8</sup> using four different questionnaires distributed in four cities in Japan, also showed that "subjective feeling of satisfaction" was most significantly correlated with health, and, as they say, "might work to cover shortage of other resources."<sup>8</sup>

The importance of thriving is also reflected in other investigations where, in spite of different definitions, it has been proven to play a prominent role. In Denmark, for instance, E. Pedersen has emphasized in his different works<sup>9</sup> the importance of thriving in the working environment, and has shown that a person's expectations and the fulfillment of these determine the thriving of the person. The studies made by O. Berg in southern Greenland show that there is a connection between morbidity, satisfaction, and hous-

ing conditions, which connection O. Berg related to the special living conditions in this part of arctic Denmark.<sup>10, 11</sup>

In the present study the importance of psychological factors for health is strengthened by the fact that morbidity for adults was predicted by their dissatisfaction with the area of residence, the dwelling, and the partner's occupation. These factors, as well as some habits of the parents (e.g., the frequency of taking a shower) and the physical and psychological contact within the family group (number of sleeping rooms, older siblings, etc.), also influenced the morbidity of the children. In the light of these findings, morbidity appears to be more dependent on psychological factors than on technical and social standards.

The predictor "fatiguing work in the dwelling," which in this study has appeared as a predictor for morbidity, is difficult to estimate; it may reflect many factors and may be in itself partly a causal factor. However, whenever poor housing standard was demonstrated as an important predictor for morbidity, the factor "fatiguing work in the dwelling" may be a causal factor in this relation. This applies especially to Districts Five and Six, where housing standards are poorest, and which more often than not are inhabited by older people.

Overcrowding, i.e., more than 1.5 individuals per room, including the kitchen, could not be demonstrated to have an effect since 0.7 was the highest number found for this factor. The effects of overcrowding by other definitions, such as only one child in families living in one- or two-room apartments,<sup>6</sup> have not been evaluated. The study did not indicate increased morbidity for children with increasing size of the family. Furthermore, in contrast to Christensen,<sup>6</sup> no correlation was found between morbidity and the area of the dwelling. On the contrary, the morbidity of the youngest children increased with the number of rooms used for sleeping.

Almost all other of the 109 different parameters investigated, like civil status, sex, education, and occupation, showed no important statistical associations, with one exception: the total yearly income of the family. This only had influence as a secondary predictor for morbidity, during the last month of the investigation, of adults who had a better housing standard.

The negligible effects of tobacco and alcohol must be evaluated in the light of the fact that morbidity in this study covers morbidity in general. Furthermore, the influence of parents' tobacco smoking on the morbidity of the youngest children of 1-4 years of age, found by D.J. Hammer et al.,<sup>12</sup> could not be confirmed in our study. The relative influence of tobacco and alcohol on specific symptoms and diseases might give other results but was not evaluated in this study.

By and large this study indicated the importance of thriving for the health of people. It should be pointed out that people in some old-fashioned districts fight for the right to stay and to preserve the present environment of the houses, while at the same time up to 50% of people in new flats in the suburbs express a wish to move.<sup>18</sup> This fact seems to indicate that modern planning in Copenhagen

has failed to provide an environment acceptable to people of our time, which was the original intention.

## Conclusion

The results obtained indicate that measures to improve the public health should also aim at increasing the thriving of people in their environment, at home, in their area of residence, and at work, or at least at protecting them from processes that might in any respect disturb their thriving. Community health planning and education should to a greater extent attend to housing standards, spare-time facilities, and efforts to improve personal hygiene.

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Melia, R.J.W., Florey, C.V., Altman, D.G., Swan, A.V. "Association between gas cooking and respiratory disease in children" British Medical Journal 2:149-152, 1977.

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A total of 5758 children age 6 to 11 years from 28 randomly selected areas of England and Scotland were examined. In an analysis of the effects on health of possible indoor pollutants, boys and girls from homes in which gas was used for cooking were found to have more cough, "colds going to the chest", and bronchitis than children from homes where electricity was used. The girls also had more wheeze if their families used gas for cooking. This "cooking effect" appeared to be independent of the effects of age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating. It was concluded that elevated levels of oxides of nitrogen arising from the combustion of gas might be the cause of the increased respiratory illness.

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## Association between gas cooking and respiratory disease in children

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### Summary

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### Introduction

Respiratory disease is a major cause of childhood morbidity. Episodes of respiratory disease have been said to predispose

children to acute respiratory disease in early adulthood,<sup>1</sup> which may in turn predispose them to later chronic respiratory disease—a major cause of morbidity and mortality among older people in the United Kingdom.<sup>2</sup> The burden of chronic respiratory disease might be reduced if environmental hazards known to be associated with acute respiratory disease in childhood were altered or removed.

Outdoor air pollution has been repeatedly shown to be related to the prevalence of respiratory illness in children<sup>3-6</sup> and our data have suggested that the relationship may exist even at relatively low levels of pollution.<sup>7</sup> We examine here the relation between respiratory illness and indoor air pollution arising from cooking fuels. The two fuels predominantly used in the home for cooking are electricity and gas. The former causes negligible pollution, but the latter gives rise to a range of pollutants on combustion.

### Methods

This project was part of a larger study of the health and growth of primary schoolchildren which started in 1972. Twenty-two employment exchange areas in England and six in Scotland were selected from a total of 547 areas by stratified random sampling so that poorer areas were proportionately better represented. Details of the sampling method have been published elsewhere.<sup>8</sup>

The study population consisted of all children aged 6 to 11 in selected primary schools within each of the 28 areas who were followed up in 1973. During this year questions on respiratory illness and the type of fuel used for cooking in the home were added to the questionnaire. Out of 9124 white children seen in 1972 7851 were re-examined in 1973.

Information about respiratory symptoms experienced during the previous 12 months and episodes of bronchitis and asthma was requested in a self-administered questionnaire completed by the children's parents or guardians.<sup>9</sup> The question about the cooking fuel used at home was: 'Do you cook by electricity, gas, coal, other (if other, please specify)? There was a similar question for the main fuel used for heating and other questions to elicit socioeconomic information. The children were classified according to their fathers' occupations into the six social class groups defined by the Registrar General.<sup>10</sup> No questions were asked about parental smoking habits.

Outdoor smoke and sulphur dioxide ( $\text{SO}_2$ ) were sampled over 24-hour periods at or near the study schools in 10 of the areas, using the daily smoke  $\text{SO}_2$  sampler.<sup>11</sup>

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Of the 7851 children 214 were excluded from the analysis because they came from homes in which coal or a mixture of fuels was used for cooking. There was no information on cooking fuels for 89% of the remaining 7637 children, which left 6747 children who came from homes in which either electricity or gas only was used for cooking. Data (on age, sex, social class and responses to all six questions on respiratory symptoms and diseases) were complete for 5754 of these children: 3264 lived in homes where electricity was used for cooking and 2554 in homes where gas was used.

## Results and comment

### SIMPLE PREVALENCES

In each case the prevalence of each respiratory symptom and disease was higher in boys and girls from homes where gas was used (table I). The differences in prevalence between the two groups of children were significant ( $P < 0.05$ ) for bronchitis, day or night cough, and colds going to the chest in both sexes and, in girls, for all other symptoms. Prevalence rates were higher in boys than in girls.

### COMPARISONS OF RESPIRATORY ILLNESS ALLOWING FOR RELATED FACTORS

The prevalence of symptoms and diseases in the children was greater in the lower than in the upper social classes and declined with age. Since the proportion of children in social classes I, II, and III (non-manual) was higher among those from homes where electricity was used for cooking (table II) and there were minor differences in age between the two groups of children, it was important to allow for the effect of these factors in the analyses. Moreover, the analysis shown in table I did not take into account the fact that some children had more than one symptom or disease. Fortunately a new computer package—GLIM (Generalised Linear Interactive Models)—which has a facility for fitting log-linear models<sup>11</sup> to frequency data has become available. These models are particularly suitable for analysing the relation between a set of factors and a categorical response when the response cannot be sensibly represented on a quantitative scale. This is a considerable advantage over more commonly used methods, which require the construction of a score, with associated assumptions of normality and the necessity for intervals on the scale to have some quantitative interpretation.

To carry out this analysis we prepared a set of response categories using histories of bronchitis, colds going to the chest, and the three symptoms (day and night cough, morning cough and wheeze). Children reported to have asthma were excluded from the analysis. Although the analysis technique did not require it, we used a sequence of categories related to increasing severity of respiratory illness to simplify the interpretation. Because there was no obviously correct way of doing this we chose the simplest. A count of the positive responses to the five questions on symptoms and diseases was used

to define the following four categories: (1) no symptom or disease; (2) one symptom or disease; (3) two symptoms or diseases; (4) three or more symptoms or diseases.

Since the prevalence of symptoms and disease differed between the sexes, boys and girls were analysed separately. Within each sex the children were divided into eight subgroups, according to social class (III (non-manual) or above; or class III (manual) or below); age (below 8 years; or 8 years and over); and the type of cooking fuel used. Within each subgroup the distribution of the children among the four categories of respiratory illness was determined (table III). These distributions for all the subgroups were then analysed using the log-linear model facility in the general linear model-fitting program<sup>12</sup> to test whether there were systematic and consistent differences between them related to social class, age, or types of fuel. This technique had obvious advantages over the relative-risk approach, with its requirement that the response categories be compressed into a dichotomy, with a consequent loss of information.

As expected, the analyses for both sexes showed that the proportion in the more severe categories of respiratory illness was greater in the lower social class group than the higher group ( $P < 0.03$ ) and greater for younger than for older children ( $P < 0.01$ ). An association between greater severity of illness and the use of gas for cooking was also found after allowing for the effects of social class and age ( $P < 0.07$  for boys;  $P < 0.001$  for girls). In other words, in the gas cooking groups the proportion of children in the more severe illness categories increased at the expense of those in the less severe categories. Thus if girls aged under 8 years and from social class III (manual) or below are taken as an example, 11% of those from homes using electricity had two or more diseases or symptoms compared with 16% of those from homes using gas.

Effects due to latitude and the degree of urbanisation might also have biased the results, so the analysis was extended to include these factors. To represent latitude the areas were grouped into three regions: Scotland, England north of the line joining the Bristol Channel to the Wash, and England south of this line. Urban and rural areas were defined according to whether they had a population density above or below 20 people per hectare. As this extended analysis was too large for our computer facility, urban and rural areas were analysed separately and the respiratory illness categories 3 and 4 combined into one. This also helped to ensure adequate numbers in each category within the 40 subgroups.

Allowing for the effect of these factors in the analysis made no difference to the direction of the relationships of illness severity with age and social class, although the associations did not always reach statistical significance. A relation with latitude did emerge, but this seemed to depend on the degree of urbanisation. For rural areas there was some evidence, confined to girls, that there was more illness in southern England. For urban areas, on the other hand, the proportion of children in the more severe categories was highest in northern England and lowest in the south ( $P < 0.001$  for boys; and  $P < 0.005$  for girls). This finding is difficult to explain simply, although it could be argued that latitude has no effect in rural areas—that is the significant result for the girls was a chance one, while in the urban areas the

TABLE I—Prevalence (%) of respiratory symptoms and diseases during last 12 months in boys and girls according to type of fuel used for cooking in the home

Symptoms and diseases	Boys			Girls		
	Electricity	Gas	P*	Electricity	Gas	P*
Non-hits	3.1	9.7	<0.001	3.0	4.7	<0.001
Day or night cough	5.4	4.5	<0.001	3.9	8.7	<0.001
Morning cough	3.0	4.3	<0.07	2.0	4.1	<0.001
Cold going to chest	23.0	26.4	<0.02	10.8	24.1	<0.006
Wheeze	10.3	11.2	0.6	9.7	8.6	<0.005
Asthma	1.4	2.7	0.2	1.0	1.4	0.2
No of children	1645	1274		1996	1240	

\*Probability value for difference between prevalence rates,  $\chi^2$  test.

TABLE II—Distribution of social class in each cooking group

Social class:	I	II	III (non-manual)	III (manual)	IV	V	Total
No (%) in electricity group	151 (4.7)	576 (18.0)	333 (10.4)	1604 (50.2)	436 (13.6)	100 (3.1)	3264 (100)
No (%) in gas group	83 (3.2)	319 (12.5)	102 (7.5)	1373 (53.6)	406 (15.6)	181 (7.1)	2554 (100)
No (%) of children (total)	234 (4.1)	895 (15.5)	435 (7.5)	2977 (51.8)	842 (14.6)	281 (4.9)	5758 (100)

TABLE III—Percentage of boys and girls classified by respiratory illness category, social class, age, and type of fuel used for cooking in the home

Respiratory illness category*	Social classes I-III (non-manual)				Social classes III (manual) - V			
	<8 years		8+ years		<8 years		8+ years	
	Electricity	Gas	Electricity	Gas	Electricity	Gas	Electricity	Gas
1	74.4	71.9	70.2	76.7	70.1	62.5	75.0	71.0
2	14.6	14.6	13.1	15.9	17.0	21.3	15.7	17.7
3	4.0	9.0	5.2	3.2	6.9	4.4	5.5	6.3
4	3.0	2.1	2.5	4.2	5.4	7.8	3.8	5.0
Total†	100 (203)	100 (88)	100 (105)	100 (100)	100 (375)	100 (309)	100 (575)	100 (654)
Girls								
1	77.6	69.6	61.9	80.4	64.2	66.5	82.2	72.2
2	14.6	17.9	14.2	14.4	21.1	17.5	12.9	15.2
3	4.1	8.9	2.0	3.7	7.4	9.2	9.7	6.6
4	2.1	3.6	1.9	1.1	3.3	6.2	1.8	2.7
Total†	100 (171)	100 (112)	100 (91)	100 (107)	100 (343)	100 (337)	100 (674)	100 (623)

\*See text. †Numbers of children are given in parentheses, but they do not add up to 5750 as asthmatics have been excluded.

effects followed the pattern one might have expected given the more intense industrialisation of the north.

The association between the distribution among the respiratory illness categories and the type of cooking fuel was still apparent even after these extra factors were taken into account. The proportion of children with more than one disease or symptom was still higher among those from homes where gas was used for cooking. But this association was significant only for girls in urban areas ( $P = 0.03$ ), though the trend was in the same direction for both sexes in urban and rural areas. In fact for the girls in rural areas and the boys in urban areas the association was not far from significance ( $P = 0.10$ ).

Although we allowed for the effects of latitude and degree of urbanisation by classifying the areas into six groups it was still possible that some of the cooking effect could have been explained by the differences between the areas within each group. As it was impractical to divide the children into still more sub-groups we expanded the area groups to 26 at the expense of the respiratory illness categories, which were reduced to two (those with and those without symptoms or diseases). Using a logistic transformation of the proportion of children in the illness categories as the outcome variable, we obtained very similar results to our first log-linear model analysis. After allowing for the effects of social class, age, and area, there was a significant association of symptoms and diseases with the use of gas for cooking in girls ( $P = 0.05$ ), and, although the effect did not reach significance in boys ( $P = 0.30$ ), it was in the same direction.

We also considered other factors that might have affected the comparisons, such as the number of siblings, overcrowding in the home, fuels used for heating and atmospheric smoke and  $SO_2$  levels. Data for these variables were, however, missing for many of the children, so only very small numbers remained within the necessary subgroups. Thus the results from these analyses were not so conclusive and will need confirmation by study of the more complete data now being collected. None the less, when these factors were taken into account, the proportion of children with one or more respiratory symptoms or diseases remained higher in both boys and girls from homes where gas was used. This approached significance in girls ( $P = 0.10$ ), but not in boys.

## Discussion

We have shown that children from homes where gas is used for cooking have a higher prevalence of respiratory symptoms and disease. This may be due to pollution of the indoor atmosphere by the products of gas combustion, but other factors associated with gas cooking and respiratory disease may still underlie the findings. So far as possible we have made allowances for most of the obvious factors. Although the grouping of social class which we had to use was rather broad, the differences in the use of electricity and gas between the social class groups were quite small (table II). On the other hand, we could not exclude family smoking habits in the analysis, but the known relation between smoking and social class<sup>19</sup> has allowed us to avoid at least some of the potential bias from this source. It

seems unlikely that within our social class groups there was a higher prevalence of smoking in homes where gas was used for cooking.

The main constituents in the emissions from a gas cooker are  $N_2$ ,  $O_2$ ,  $CO_2$ , and water vapour, with small amounts of  $CH_4$ ,  $C_2H_6$ , and other hydrocarbons,  $CO$ ,  $NO$ ,  $NO_2$ , and various aldehydes. Other pollutants, such as  $HF$ ,  $HCl$ , and  $HBr$ , can be formed as a result of residual aerosol spray vapours in combustion air passing through the flame on the cooker.

Reports<sup>11,12</sup> indicate that the concentrations of oxides of nitrogen emitted from gas cookers are above those recommended in the US Primary Air Quality Standards<sup>16</sup> and Emergency Episode Criteria Guidelines.<sup>17</sup> The maximum level recommended for the annual arithmetic mean is 0.05 ppm, and the alert levels for the 24-hour and one-hour averages are 0.15 ppm and 0.6 ppm respectively. Derwent and Stewart<sup>11</sup> have reported that the concentrations of oxides of nitrogen taken as a whole that are emitted from a gas cooker range from 8 to 33 ppm. Wade *et al.*<sup>12</sup> found that over a two-week period the average concentration of  $NO_2$  in kitchens where a gas cooker was used was over 0.05 ppm, the maximum recommended ambient level. They also showed how the concentration in different parts of the home fluctuated with the use of the cooker, and reached average levels of over 0.15 ppm for two hours in the kitchen.

Little has been published about the effects of these gases on human health. Reports of human exposure have been confined to agricultural and industrial accidents, in which adults have been suddenly exposed to very high levels of  $NO$  and  $NO_2$ , with resulting extensive pulmonary oedema. These levels were much higher than those emitted by gas cookers.<sup>11,12</sup>

Information on the effects on health of low-level exposure to  $NO$  and  $NO_2$  has come from animal and epidemiological studies. Mice have been shown to have an increased susceptibility to infection by *Klebsiella pneumoniae* when first exposed to concentrations of  $NO_2$  of 3.4 to 25 ppm<sup>18</sup> for about two hours. Shy *et al.*, reporting some of the Community Health and Environmental Surveillance System studies,<sup>11</sup> attributed a modest decrease in the respiratory function of children aged 7-8 to exposure to a yearly average concentration of outdoor  $NO_2$  of 0.08 ppm. Their measurements of  $NO_2$  have since, however, been shown to be highly correlated with  $SO_2$  concentrations, and the effects of the two pollutants could not be separated.<sup>19</sup> We have found only one report of studies similar to ours, which were carried out in families living in a suburb of Columbus, Ohio, and on Long Island, New York.<sup>21</sup> In contrast to our findings, the authors found no association between respiratory disease and the use of electricity or gas for cooking.

$SO_2$  is also given off during the burning of gas and is potentially harmful to health. But the sulphur content of gas is legally limited and the levels of  $SO_2$  produced are likely to be very much

lower than those currently believed to have adverse effects on health. Thus it seems unlikely that this pollutant would have caused our findings.

Possibly the combustion products of coal gas and natural gas differ in some relevant way. We could not separate the effects of the two types of gas because most of the study areas underwent a changeover from town to natural gas during 1973, and the children were exposed to the products of combustion of both gases.

The relation between gas cooking and respiratory disease seems to be stronger and more consistent for girls than for boys, as would be expected if girls spent more time in the family kitchen. If this is the case, and the difference between the sexes is purely the result of differing exposure, it seems likely that increased ventilation might be sufficient to dispel any risk.

Nevertheless, detailed research is required to determine whether the relation we have found is really due to a direct effect of the products of gas combustion on the respiratory tract before more complicated measures for the protection of health are considered.

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# Dextrostix-Eyetone in the insulin hypoglycaemia test

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## Summary

The Ames Dextrostix-Eyetone system was evaluated for monitoring the blood glucose concentration during insulin-induced hypoglycaemia. The results agreed well with laboratory values for plasma glucose, obtained by an orthotoluidine method, and the method was practicable as a bedside technique. In two cases quick results obtained with the Eyetone enabled the insulin tolerance test to be interrupted to prevent severe hypoglycaemia before the clinical indications were obvious. The extra time and effort required were minimal, and its value

seems to far outweigh the disadvantage of the extra work entailed. Nevertheless, care in using the system was important, and the operator must familiarise himself with the system before the most reliable results can be obtained.

## Introduction

The best validated test of pituitary growth hormone (GH) release in man is the insulin tolerance test (ITT), which allows GH and ACTH production by the pituitary to be assessed simultaneously.<sup>1</sup> The test is especially useful as thyrotrophin-releasing hormone (TRH) and gonadotrophin-releasing hormone (GRH) may be given at the same time so that prolactin and gonadotrophin secretion can be assessed simultaneously.

Adequate hypoglycaemia must be achieved before the ITT can be considered to be satisfactorily completed. Hypoglycaemia is generally recognised from the clinical signs (such as sweating) and, retrospectively, by seeing that the plasma glucose concentration has fallen by at least 50% from the fasting value and is below 2.8 mmol/l (50 mg/100 ml) at the nadir. Because of this and of the danger of severe hypoglycaemia, especially in young children, there have been extensive searches for other

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Melia, R.J.W., Florey, C.D., Chinn, S. "The Relation between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking I. Results from a National Survey" International Journal of Epidemiology 8(4): 333-338, 1979.

SUMMARY: The relation between the prevalence of respiratory illness and the use of gas for cooking in the home has been investigated in a 5 year longitudinal study of primary schoolchildren from England and Scotland. 4827 boys and girls aged 5 to 10 years from 27 randomly selected areas were examined in 1977, the last year of the study. The prevalence of one or more respiratory symptoms or diseases was higher in children from homes where gas was used for cooking than in those from homes where electricity was used. The association appeared to be independent of age, sex, social class, number of cigarette smokers in the home and latitude but it was only found in urban areas (for boys  $p < 0.005$ ; for girls  $p \leq 0.08$ ). In children aged from 6 to 7 1/2 in 1973 who were followed until the last year of the study there was some indication that the association between respiratory illness and gas cooking may have disappeared as the children grew older. However this trend was not obvious in the other age groups who were followed for 2 to 4 years. The evidence of an association between gas cooking and respiratory illness in 1977 supports results for 1973 presented in an earlier report while the cohort results provide some indication that the association may disappear as children grow older.

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# The Relation between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking

## I - Results from a National Survey

R J W MELIA, C du V FLOREY and S CHINN

Melia R J W (Department of Community Medicine, St. Thomas's Hospital Medical School, London SE1), Florey C du V and Chinn S. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking I - results from a national study. *International Journal of Epidemiology* 1979, 8: 333-338.

The relation between the prevalence of respiratory illness and use of gas for cooking in the home has been investigated in a 5 year longitudinal study of primary schoolchildren from England and Scotland. 4827 boys and girls aged 5 to 10 years from 27 randomly selected areas were examined in 1977, the last year of the study. The prevalence of one or more respiratory symptoms or diseases was higher in children from homes where gas was used for cooking than in those from homes where electricity was used. The association appeared to be independent of age, sex, social class, number of cigarette smokers in the home and latitude but it was only found in urban areas (for boys  $p < 0.005$ ; for girls  $p = 0.08$ ). In children aged from 6 to 7% in 1973 who were followed until the last year of the study there was some indication that the association between respiratory illness and gas cooking may have disappeared as the children grew older. However this trend was not obvious in the other age groups who were followed for 2 to 4 years. The evidence of an association between gas cooking and respiratory illness in 1977 supports results for 1973 presented in an earlier report while the cohort results provide some indication that the association may disappear as children grow older.

We previously reported an association between the prevalence of respiratory symptoms and disease, and the use of gas for cooking using data from a national study of respiratory illness in primary schoolchildren (1). We believed that indoor air pollution from nitrogen dioxide ( $\text{NO}_2$ ) formed during the combustion of gas might have been the cause of this association because this pollutant has been shown to increase susceptibility to respiratory infection in animals (2). In this series of 3 papers we present an analysis of more recent data from our national study and also the results of an investigation of the relation between children's respiratory illness and  $\text{NO}_2$  levels in the home (3, 4).

As the national study was longitudinal and the association had only been reported for children present in the first year, 1973, we examined the

data collected over the 4 following years. Results are reported here for 2 groups of children: those aged 5 to 10 years who were present in 1977 but not 1973 (cross-sectional analysis), and those present in 1973 who were followed-up in subsequent years (cohort analysis). Unlike previous years, in 1977 information was collected on the number of people who smoked cigarettes, cigars and pipes in the home. Additional information was collected on gas water heaters and use of pilot lights on gas cookers as it was thought that these might contribute to the concentration of  $\text{NO}_2$  in the home.

### METHODS

Children aged 6 to 11 years who attended schools in 28 randomly selected areas of England and Scotland were examined annually from 1973 to 1977. The areas were selected from 597 employment exchange areas by stratified random sampling and a socio-economic index was used to obtain a high proportion of poor areas. Details of the method

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TABLE 1 *Crude prevalence (%) of respiratory symptoms and diseases in boys and girls by type of fuel used for cooking in the home*

Symptoms and Diseases	Boys		P*	Girls		P*
	Electricity	Gas		Electricity	Gas	
Morning cough	2.1	3.1	<0.20	2.4	3.3	p>0.20
Day or night cough	4.2	6.3	=0.02	4.4	4.7	p>0.20
Wheeze	10.1	10.1	p>0.20	6.2	7.1	p>0.20
Colds going to chest	23.2	26.4	p<0.10	19.6	23.1	p<0.05
Asthma	2.4	2.4	p>0.20	1.0	1.2	p>0.20
Bronchitis	3.2	3.6	p>0.20	2.2	2.4	p>0.20
Any respiratory illness	26.3	31.2	p=0.01	23.1	26.5	p=0.07
No. children	1549	909		1468	901	

\* Probability value of difference between prevalence rates  $\chi^2$  test

of sampling are described elsewhere (5).

In 1977, however, schools from 4 areas were unable to participate and other state schools in the areas were selected. A further 4 areas declined to take part at all and nearby areas with the same socio-economic index were substituted. One of the new areas was not ready to join the study in 1977 so the children came from 21 English and six Scottish areas. The age range was extended in 1977 to include 5 year olds.

Information about each child and the home environment came from a questionnaire completed by the child's mother or other guardian. Six questions used in the previous years of the study were asked about cough, wheeze, colds going to the chest, and the number of attacks of asthma and bronchitis experienced by the child during the previous 12 months. Other questions were asked about the type of fuels used for cooking and heating in the home, the presence of gas water heaters, the use of pilot lights on gas cookers, and the number of people in the household who smoked cigarettes (at least 5 a day) and cigars or pipes regularly. The father's occupation was coded into social class using the Registrar General's classification (6) and the numbers of bedrooms and people in the household were used to obtain a measure of overcrowding.

#### *Population for 1977 Cross-Sectional Analysis*

9925 children were included in the study in 1977 but 1330 10 to 11 year olds were excluded because they had also been present in 1973 and we wished to study a different group of children from those among whom the effect of gas cooking had first been found. Out of the remaining 8595, 271 were omitted because their ethnic group was either not

known or known to be non-Caucasian, 88 because their age was not known and 261 because they were aged less than 5. 5008 (63%) of the remaining 7975 children had complete information on the 6 respiratory symptoms and diseases, their father's social class, the number of cigarette smokers in the home and type of fuel used for cooking. 181 of these were excluded because they did not come from homes where only electricity or only gas was used for cooking. As the numbers of cigar and pipe smokers in the home tended to be associated with the number of cigarette smokers we used only the latter in the analysis as a general indicator of smoking in the home. The analysis was carried out on 3017 children from homes with an electric cooker and 1810 from homes with a gas cooker. This 62% sample of the total 7794 children eligible for analysis showed no significant difference in mean height or weight by age from the remaining 38% whose measurements had also been taken. For 2 additional analyses 98% of the 4827 children had information on gas water heaters and 99.6% of those from homes with a gas cooker had data on pilot lights.

#### *1973 Cohort Analysis*

Children first examined in 1973 left the study when they left primary school at age 11 or 12, or if they moved away from their area. They could be divided into 5 cohorts according to the number of completed years for which they remained in the study (less than 1 to 4). In our analysis we have considered only children who had been followed-up for at least one year and whose mother had reported the use of the same cooking fuel in each year that their child was studied. There were insufficient numbers for

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analysis of those who reported a change in cooking fuel. 5758 (73%) of the 7851 Caucasian children aged 6 to 11 years who were included in the study in 1973 had complete information on sex, social class and the 6 respiratory symptoms and diseases, and came from homes where only gas or electricity was used for cooking. Of these 5758, 2408 (42%) had data for full follow-up: 791 children aged 9.5 to 10.9 (14%) were followed up with complete information for one year until 1974, 578 aged 8.5 to 9.4 (10%) until 1975, 502 aged 7.5 to 8.4 (9%) until 1976 and 537 aged 6 to 7.4 (9%) until 1977.

#### CROSS-SECTIONAL RESULTS FROM 1977

##### Crude Prevalences

Only the prevalences of day or night cough in boys ( $p = 0.02$ ) and colds going to the chest in girls ( $p < .05$ ) were found to be significantly higher in children from homes where gas was used for cooking compared with children from homes where electricity was used. Although none of the other symptoms or diseases appeared to have a statistically significant association with gas cooking the prevalences of all symptoms and diseases in girls and of morning cough, colds going to the chest and bronchitis in boys appeared to be higher in children from homes with gas cookers.

As no particular symptom or disease showed a strong association with type of cooking fuel in either sex and the responses to the 6 respiratory questions were inter-related we grouped the various

responses to the 6 respiratory questions by a method similar to that used in our previous paper (1). The children were grouped according to whether they had none, or one or more symptoms or diseases. In both sexes this prevalence was higher in children from homes where gas was used for cooking than in those from homes where electricity was used ( $p = 0.01$  in boys,  $p = 0.07$  in girls).

##### Prevalence and related factors

Several interfering factors needed to be considered in the analysis. The most obvious of these were age and social class (Table 2). Within each age group (less than 8, and 8 or more) and each social class group (I to III (non-manual), and III (manual) to V) the risk of having one or more respiratory symptoms or diseases in homes with gas cookers relative to the risk in homes with electric cookers was greater for all children except girls aged 8 or more from the manual social classes. The weighted relative risk (7) across these groups in homes with gas compared with homes with electric cookers was 1.25 for boys ( $p < 0.05$ ) and 1.19 for girls ( $p = 0.07$ ). The relative risk in boys was similar to that for boys aged 6 to 11 who had been examined in 1973 (1.29,  $p < 0.05$ ) but in girls the relative risk was smaller in 1977 than 1973 when the value was 1.40 ( $p < 0.001$ ).

In addition to age and social class we also considered the number of cigarette smokers in the home. The number of smokers was associated with

TABLE 2 Percentage of boys and girls classified by the number of respiratory symptoms and diseases that they were reported to have, social class, age and type of fuel used for cooking. Risk of having respiratory illness in homes with gas cooking relative to risk in homes with electric cooking also given.

SEX	No. Respiratory Symptoms or Diseases	SOCIAL CLASS I-III (non-manual)				SOCIAL CLASS III (manual) - V			
		< 8 Years		> 8 Years		< 8 Years		> 8 Years	
		Electricity	Gas	Electricity	Gas	Electricity	Gas	Electricity	Gas
BOYS	None	72.6	68.3	80.8	71.7	67.2	63.3	76.4	73.1
	1 or more	27.4	31.7	19.2	28.3	32.8	36.7	23.6	26.9
	TOTAL †	100	100	100	100	100	100	100	100
		(277)	(145)	(286)	(113)	(485)	(313)	(501)	(338)
	Relative Risk	1.2		1.7*		1.2		1.2	
GIRLS	None	75.6	72.4	85.2	81.4	72.2	63.7	78.5	81.5
	1 or more	24.4	27.6	14.8	18.6	27.8	36.3	21.5	18.5
	TOTAL †	100	100	100	100	100	100	100	100
		(291)	(134)	(243)	(118)	(497)	(336)	(437)	(313)
	Relative Risk	1.2		1.3		1.5*		0.8	

\*  $p < 0.05$ . † number of children given in brackets

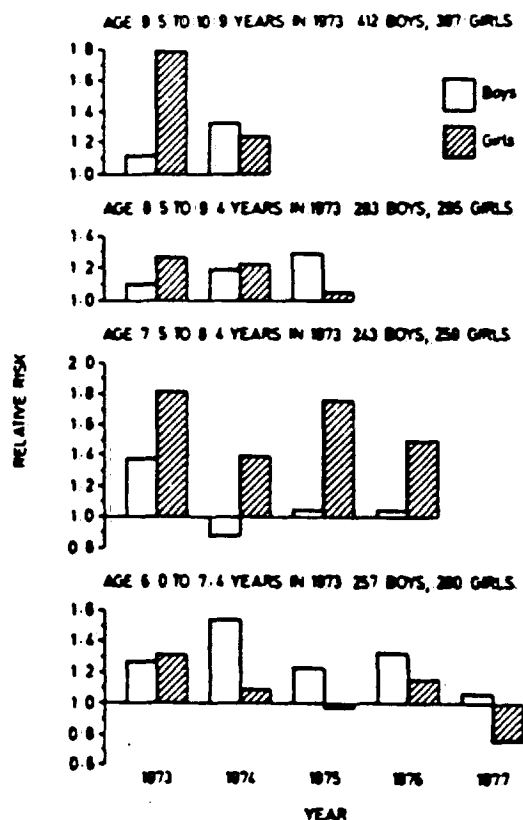


FIGURE  
The relative risk for respiratory illness in children from gas cooking homes compared with children from electric cooking homes is given by sex and year of examination for four cohorts defined by age at entry into the study in 1973.

the use of gas for cooking within manual but not non-manual social classes (Table 3). Furthermore the degree of urbanisation and location of the study areas defined by latitude (Scotland, and England divided into north and south by a line joining the

Bristol Channel to the Wash) were included in the analysis because in 1973 the association between respiratory illness and gas cooking was found to be most consistent in urban areas in the north of England.

The relation between these factors and the prevalence of respiratory illness was examined by fitting a log-linear model using a method of analysis described in greater detail in our earlier paper (1). We first divided the children into 1 of 2 categories according to whether they had none, or one or more symptoms or diseases. We then divided the children by age, sex, social class and type of cooking fuel as shown in Table 2, into rural and urban areas (less than 20, and 20 or more persons per hectare respectively) and the 3 divisions of latitude. The model was fitted separately for boys and girls, and for rural and urban areas as the computer program did not allow space for the full model.

An association between gas cooking and respiratory illness was found independent of the effects of the other factors in urban areas (for boys  $p < 0.005$ , for girls  $p = 0.08$ ) but not rural ones. For girls in rural areas, however, there appeared to be an association in the younger age group. In contrast the effect of number of smokers in the home was only significant in rural (for both sexes  $p < 0.005$ ) but not urban areas. As might have been expected the prevalence was higher in the younger than the older age groups ( $p < 0.05$ ) in all 4 analyses and tended to be higher in the manual than the non-manual social classes although this relation was not always significant. An effect of latitude was only found in girls from urban areas ( $p < 0.05$ ), the prevalence being highest in the north and lowest in the south of England.

We extended the 1977 analysis to allow for the effects of various other factors: overcrowding, type of fuel used for heating in the home and outdoor levels of smoke and sulphur dioxide in each area. Only 1032 boys and 950 girls could be included in

TABLE 3 Percentage of children living in homes with no cigarette smokers and one or more smokers by the father's social class and type of fuel used for cooking in the home.

No Cigarette Smokers	Social Classes I-III (non-manual)		P	Social Classes III (manual) - V		P
	Electricity	Gas		Electricity	Gas	
None	55.4	58.8		38.3	28.5	
1 or more	44.6	41.2	= 0.20	61.7	71.5	<0.001
TOTAL *	100 (1097)	100 (510)		100 (1920)	100 (1300)	

\* Number of children given in brackets.

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## RESPIRATORY ILLNESS IN SCHOOLCHILDREN

337

TABLE 4 Crude prevalence (%) of having one or more respiratory symptoms or diseases in boys and girls by presence of gas water heaters in the home and use of pilot lights on gas cookers

SEX	Presence of Gas Water Heater			Use of Pilot Light *		
	No	Yes	P	No	Yes	P
BOYS†	27.7 (2253)	33.3 (141)	< 0.20	30.8 (305)	31.4 (598)	p > 0.20
GIRLS†	23.9 (2201)	33.9 (121)	< 0.02	23.2 (310)	28.3 (590)	p < 0.15

† number of children given in brackets

\* children from homes with electric cooking excluded

this analysis so these findings must be treated with caution. However, after allowing for the various effects, respiratory illness was shown to be associated with gas cooking although only significantly so in boys (for boys  $p < 0.02$ ; for girls  $p = 0.15$ ).

Finally we examined the effects of gas water heaters and pilot lights (Table 4) but a relation could only be found between respiratory illness in girls and gas water heaters. When we fitted a log-linear model to include age, social class, and number of smokers in the home in the analysis, the association between water heaters and respiratory illness was inconsistent across the 2 social class and cooking fuel groups. However a significant association was found in girls after allowing for the effects of the other factors ( $p < 0.05$ ).

**LONGITUDINAL RESULTS FOR 1973 COHORTS**  
For the 4 cohorts of children who were followed up for 1 to 4 years, the risk of having one or more respiratory symptoms or diseases in homes with gas cookers relative to the risk in homes with electric cookers was calculated for each sex in each year that the children were examined (Figure).

In each cohort in 1973 the risk was greater in homes with gas than homes with electric cookers. In later years, as the cohorts grew older, the relative risk showed considerable variation. Although in most groups the risk was greater in homes with gas than homes with electric cookers, there were groups for whom the risk was either negligible or greater in homes with electric cookers. For each cohort there appeared to be no consistent change in the size of relative risk over time except possibly in the youngest cohort for which the relative risk tended to decline from 1973 to 1977.

**DISCUSSION**

Although the results for the children seen in 1977

were similar in many respects to those for children seen in 1973 there were differences. The effect of gas cooking seemed to be smaller in 1977 than in 1973, at least among girls and, whereas the effect had been most consistent in urban areas in the north of England in 1973, it appeared to be independent of latitude in 1977.

As the prevalences tended to be higher in 1973 than 1977 for children of the same age it is possible that children examined in the first year were predisposed to respiratory illness through the effect of some other factor and were therefore more susceptible to the effect of gas cooking. Differences in weather conditions between the 2 years would not explain these observations as the winter of 1976/77 was colder than that of 1972/73. However as the levels of outdoor air pollution from smoke and sulphur dioxide have been declining over a number of years in the United Kingdom (8) children studied in the first year may have been exposed to higher levels of outdoor air pollution during their lives than children examined in the last year. As the decline in these levels is likely to have been most marked in urban areas in the north of England this may explain why the effect of gas cooking was no longer most consistent in this type of area by 1977. Past high levels of atmospheric pollution may also have contributed to the differences in longitudinal results between the cohorts first examined in 1973.

There seems to be no obvious reason why there should be a gas cooking effect in urban areas and a smoking effect in rural areas. We can only suggest that variation in the size of effects has occurred by chance because the sample of children has been subdivided into so many small groups during the analysis. Similarly, as the effect of gas water heaters was only found in girls, a more thorough investigation would be required before drawing conclusions from this result.

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In summary we have observed an association between respiratory illness and the use of gas for cooking in 2 separate groups of children seen 4 years apart in our national study. However the relative risk for children in homes with gas cookers compared with those in homes with electric cookers appears to be smaller in 1977, at least in girls, and only significant in urban areas. There is also some evidence that the relative risk may decline as the children grow older.

#### ACKNOWLEDGEMENTS

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**2023510149**

Speizer, F.E., Ferris, B., Bishop, M.M., Spengler, J. "Respiratory Disease Rates and Pulmonary Function in Children with NO<sub>2</sub> Exposure" American Review of Respiratory Disease 121(1): 3-10, 1980.

SUMMARY: As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO<sub>2</sub> levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 ug/m<sup>3</sup>. Short-term peak exposures, which were in excess of 1,100 ug/m<sup>3</sup>, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

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## Respiratory Disease Rates and Pulmonary Function in Children Associated with NO<sub>2</sub> Exposure<sup>1-4</sup>

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### SUMMARY

As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO<sub>2</sub> levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 µg/m<sup>3</sup>. Short-term peak exposures, which were in excess of 1,100 µg/m<sup>3</sup>, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

### Introduction

There is little doubt that NO<sub>2</sub> at high concentration is associated with acute pulmonary edema and death. Silo filler's disease in which farmers are exposed to concentrations of NO<sub>2</sub> in excess of 200 ppm (376,000 µg/m<sup>3</sup>) with a resultant occurrence of acute pulmonary disease and occasionally death was described in the 1950s (1). Farmers surviving such exposures can develop pulmonary fibrosis.

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<sup>2</sup> Supported in part by grants from the National Institute of Environmental Health Sciences (ES0002, ES01108), Electric Power Research Institute Contract No. RP 1001 EPRI, and EPA Contract No. EP 68-02-3201.

<sup>3</sup> Presented in part at the Symposium on Health Effects of Nitrogen Oxides, ACS/CSJ Chemical Congress 1979, American Chemical Society, Chemical Society of

Japan, Honolulu, Hawaii and at American Thoracic Society Meeting, May 1979, Las Vegas, Nevada.  
Recently, concern over the effects of indoor exposure to lesser concentrations of NO<sub>2</sub>, both repeated short-term peak exposure and continuous low exposure, has led to studies of children (2) and housewives (3) but with inconsistent results. Melia and co-workers (2) from Great Britain reported higher rates of lower respiratory disease in school children living in households with gas cooking stoves than in those living in households with electric stoves. These differences in rates could not be explained by social class or differences in household size. However, this study did not take into account the smoking habits of the parents of these children. Subsequently, Melia and co-workers (4) found that households with gas cooking stoves had 7 times higher concentrations of NO<sub>2</sub> in the kitchen than did matched households with electric cooking devices. Similar studies in the United States found concentrations

Japan, Honolulu, Hawaii and at American Thoracic Society Meeting, May 1979, Las Vegas, Nevada.

<sup>4</sup> Requests for reprints should be addressed to Frank E. Speizer, M.D., Department of Physiology, Harvard School of Public Health, 665 Huntington Ave., Boston, Mass. 02115.

of NO<sub>x</sub>, 4 times greater in kitchens of households with gas stoves than in those with electric stoves (5). The NO<sub>x</sub> appears to be produced by the oxidation of NO when natural gas as a fuel for cooking is burned in the atmosphere. The conversion is rapid, and the NO<sub>x</sub> spreads quickly throughout the house. In contrast to the Melia study of children (2), a study of adult women living and working in households with gas stoves compared with those living and working in households with electric stoves did not show increased respiratory disease rates (3).

The results reported here were obtained as part of a long-range prospective study on the health effects of exposure to ambient levels of pollutants resulting from the burning of fossil fuels. In this study, adults between the ages of 25 and 74, selected at random from 6 communities in the eastern United States, are seen every 3 years, and school children (initially seen in grades 1 and 2) are seen annually. This report is based on the initial measurements of pulmonary function and information on respiratory diseases obtained in the children only in the 6 cities and relates these measurements to the potential indoor exposure that these children have received.

#### Methods

**Study design.** A total of 9,280 children participated in the initial surveys. These children represented 12 separate cohorts from 6 cities. Two cities were surveyed for 3 years, and a new group of first-grade school children was added each year. Thus, these cities provided 6 cohorts. Two cities were surveyed for 2 years giving 4 more cohorts, and 2 cities were surveyed once. In all the cohorts, more than 95 % of the children eligible because of their school grade were studied.

Information about the children's exposure was obtained from a questionnaire, completed by their parents, on the type of home-cooking device and home-heating fuel, the presence or absence of air conditioning, and the presence or absence of adult smokers living in the household, as well as requesting permission to perform lung function tests on the children in the schools.

Forced expiratory measurements were performed using a water-filled low-inertia recording spirometer. The children did not wear nose clips and performed the task in a sitting position, but with free movement possible. Each child had a minimum of 3 and a maximum of 8 attempts in an effort to obtain at least 3 acceptable tracings. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV<sub>1</sub>) were read from each tracing. Values were corrected to body temperature and pressure saturated with water vapor (BTPS) and summarized as the mean of the 3 best efforts that were within 170 ml of each other. Standing height in stockinged feet and weight were recorded for each child.

There were 8,866 children (95.5 % of the total seen) who were between 6 yrs and 10 yrs of age at the time of their initial survey; but the sample was reduced to 8,120 children by limiting the analyses to white children.

For each child included in the study, the lung function predicted for his or her height was computed from a regression equation determined by using the children studied in the third year of follow-up from 2 of the cities. These children, who were all within the 5 to 95 percentiles for their height corrected for age, were chosen for the standard as they provided sufficient numbers at each year of age between 6 yrs and 10 yrs (6). The difference between the observed lung function and the predicted value was obtained. These residuals were analyzed using standard analysis of variance techniques.

The reported disease rates were analyzed using log-linear models. By this means it was possible to determine significant interactions between disease, age, sex, cohort, city, and home variables. Adjusted rates were computed based on models that included the significant interactions (7).

Information regarding the differences in air quality associated with different cooking devices was obtained by setting up indoor-outdoor monitors in selected households. These households were not necessarily the homes of children in the study, but were selected to be representative of the kinds of living patterns found in each community. The homes were sampled every sixth day for 24 h, and the same time period in each city, May 1977 through April 1978, was used in all analyses. Measurements were carried out by a household sampling unit, which was placed in an "activity room," a room specifically defined as not being the kitchen or bedroom. Mass respirable particulates (mass median diameter of 3.5  $\mu$ m) were collected on millipore filters (8), and NO<sub>x</sub> was collected by a bubbler technique and measured by the EPA Reference Method, a modified sodium arsenite method (9).

The data on air pollution levels were first adjusted to take into account missing values using a linear model for day of observation and site. The influence of home variables was determined by analysis of variance, with appropriate adjustment of the residual degrees of freedom. In one household, instantaneous peak levels of NO<sub>x</sub> were monitored in the kitchen within 3 feet of a gas stove using a chemiluminescence monitor and a continuous recording.

#### Results

**Assessment of exposure to NO<sub>x</sub>.** About half of the homes in all 6 cities had gas cooking stoves, and about half had electric cooking stoves. (Six % of the homes used some other form of cooking device, alone or in conjunction with gas and/or electricity [1.9 %], or else the type of cooking device was not reported [4.1 %].) There were, however, considerable differences between cities (figure 1). The distribution of the children by home cooking device ranged from a high of 82.2 % gas cooking

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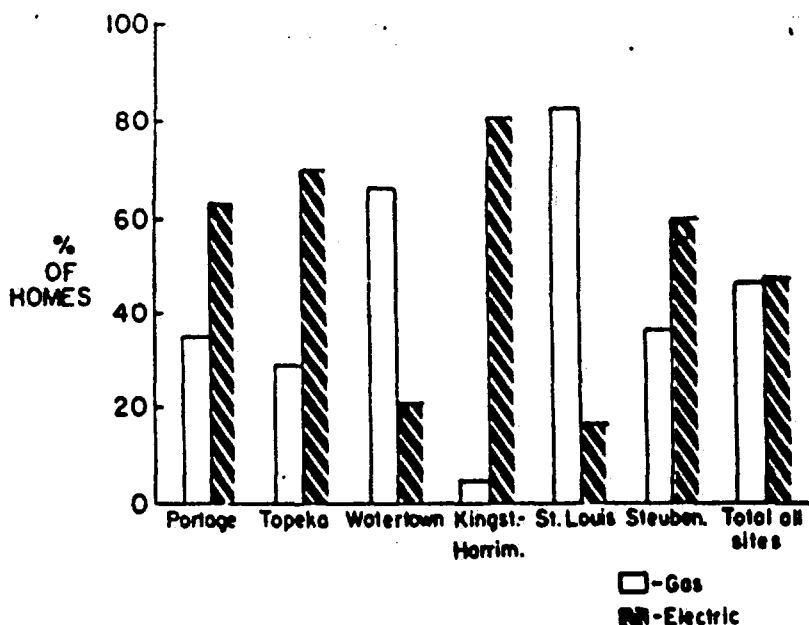


Fig. 1. Percentage of homes with gas or electric stoves, by cities.

stoves in St. Louis to a low of 4.6 % in Kingston-Harriman (figure 1).

Although the number of homes where air quality measurements were made is not large, ranging between 5 and 11 for different cities, the number of 24-h periods for which matched indoor and outdoor data are available is several hundred (table 1). The homes were divided between gas and electric cooking devices, except for Kingston-Harriman where no homes with gas stoves were studied. The results show a gradient of NO<sub>x</sub> levels in homes with electric stoves that reflect outdoor sources of NO<sub>x</sub>. High concentrations in Watertown were presumed to be caused by the proximity of homes, and therefore the monitors, to automobile traffic. A substantial increase in NO<sub>x</sub> levels in homes with gas stoves, except for Steubenville, reflects the addition of indoor sources to the outdoor level of NO<sub>x</sub>. These are 24-h integrated averages collected in an "activity room," but not in the kitchen. In some cities the daily 24-h levels encountered in some households with gas stoves exceeded the federal standard for the annual average of the 24-h NO<sub>x</sub> levels (100 µg/m<sup>3</sup>). Such levels for integrated 24-h values indicated that peak exposures must be substantially higher. This was confirmed in 1 household in which instantaneous monitoring in the kitchen produced peak levels over 1,100 µg/m<sup>3</sup> for short periods of time when the oven was in use and peaks over 500 µg/m<sup>3</sup> when a single gas burner was on (figure 2).

**Health data.** Two sets of data on the children's

health were available: data on previous illnesses reported on questionnaires completed by parents, and data from the current pulmonary function tests. The responses to 3 questions about the previous health of the children were analyzed. The questions asked if there was a history of bronchitis diagnosed by a physician, a history of serious respiratory disease before age 2, and a history of a respiratory illness in the last year.

Both the responses to these questions and the pulmonary function measurements were tested for their relationship to several household variables: type of cooking device, nature of fuel used for heating, presence of adult smokers, presence of air conditioning, and socio-economic status of the family. Socio-economic status included both occupation and educational attainment of the parents.

The 3 reported disease rates were analyzed by fitting log-linear models (7). Two of the variables, type of home-heating fuel and air conditioning, were not related to the disease rates. The social class, parental smoking, and type of cooking stove variables had differing effects on the 3 diseases when each home variable was tested alone (table 2). As the risk factors themselves were inter-related, each disease was evaluated in another log-linear analysis that included these 3 home variables simultaneously. In this multivariate analysis, the effect of the type of cooking stove had a significant association with respiratory disease before age 2, but not with the other 2 reported dis-

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TABLE 1  
INDOOR AND OUTDOOR 24-H LEVELS OF NO<sub>x</sub> IN 6 U.S. CITIES  
(MAY 1977 TO APRIL 1978)

City	Home Cooking Units			Geometric Mean Level of NO <sub>x</sub> (μg/m <sup>3</sup> )				95 Percentile Measured Level of NO <sub>x</sub> (μg/m <sup>3</sup> ) <sup>†</sup>			
	Days (no.)	Elec.		Outdoor		Indoor		Outdoor		Indoor	
		Tric (no.)	Gas (no.)	Electric	Gas	Electric	Gas	Electric	Gas	Electric	Gas
Portage*	50	8	3	7.2 (1.55) <sup>‡</sup>	5.9 (1.10)	3.6 (2.13)	14.7 (1.02)	31.8	25.4	17.6	39.3
Topeka	57	6	1	17.5 (1.25)	16.2 —	19.4 (1.26)	31.6 —	42.4	40.7	41.6	73.6
Kingston-Harriman	56	8	—	17.2 (1.25)	—	10.9 (1.43)	—	36.4	—	29.8	—
St. Louis	58	3	6	33.0 (1.17)	37.3 (1.14)	17.1 (2.01)	40.8 (1.42)	64.3	70.9	63.3	79.3
Steubenville	61	2	3	35.7 (1.00)	33.3 (1.35)	21.9 (2.59)	27.4 (2.24)	82.9	87.8	74.5	103.9
Watertown	59	2	5	49.1 (1.42)	49.2 (1.10)	41.43 (1.14)	54.3 (1.21)	101.6	106.3	95.2	116.3

\* Based on 10 month sample

<sup>†</sup> Federal 24 H standard = 100 μg/m<sup>3</sup>

<sup>‡</sup> Numbers in parentheses are geometric standard deviations

cases (table 3). Parental smoking, sex of the child, and city-cohort, but not age at the time of reporting, were also associated with respiratory disease before age 2 when other variables were taken into account. Disease rates adjusted for parental smoking, social class, and city-cohort resulted in a difference of 35/1,000 among males and 30/1,000 among females between children in homes with different cooking stoves. Lower rates were found in children of households with electric stoves for each sex in each city-cohort adjusted for parental smoking and social class (figure 3). The effects of parental smoking and city-cohort on respiratory disease before age 2 are not independent, but the

effect of the type of cooking stove appeared to be related to the other home variables.

To assess the effect of home factors on pulmonary function in these children, the difference between the expected and observed FVC and FEV<sub>1</sub> was calculated for each child. The effect of cohort (yr of study and city) and the same home variables on the residual pulmonary function were assessed by analysis of variance. Preliminary regression of lung function on socio-economic status showed no relationship. There was a significant effect ( $p < .01$ ) of cohort on both FEV<sub>1</sub> and FVC. Thus, from city to city and from year to year there were differences in the height-adjusted pulmonary

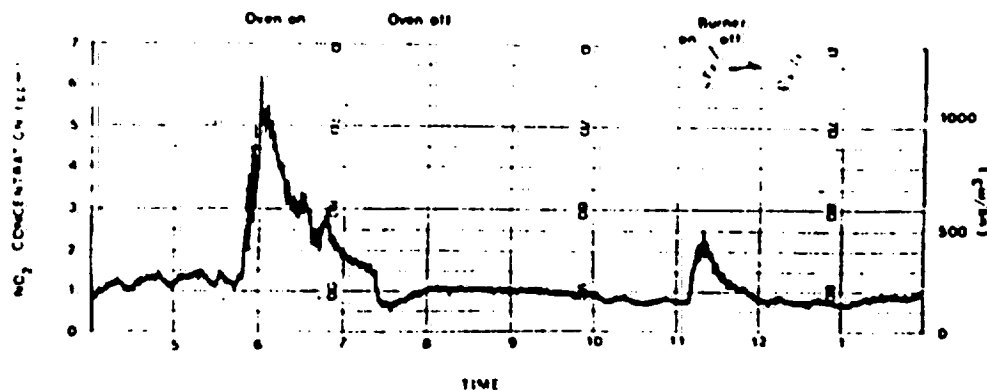


Fig. 2. Instantaneous monitoring of NO<sub>x</sub> in the kitchen, 1 meter from gas stove. Numbers along the abscissa represent hrs in the day through 1 A.M. No venting was used.

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TABLE 2  
SINGLE FACTOR ODD RATIOS (OR) AND 95% CONFIDENCE LIMITS (CL)  
FOR HOME VARIABLES AND REPORTED DISEASE RATES

		Social Class (Low/High)	Parental Smoking (Some/None)	Home Cooking (Gas/Electric)
History of doctor-	OR	0.97	1.00	0.88
diagnosed bronchitis	CL	.86-1.08	.84-1.26	.79-0.91
Serious respiratory	OR	1.13	1.32	1.12
illness before age 2	CL	1.01-1.26	1.12-1.87	1.00-1.26
Respiratory illness in the	OR	1.13	1.19	0.94
last year	CL	1.05-1.22	1.02-1.39	.88-1.05

function levels in these children, after adjusting for city-cohort effects. There were no significant associations between the presence of air conditioning in the home and lung function measurements (table 4). Although the association between parental smoking and FVC was significant at the 5 % level, with an average range of 15 ml, the result was the opposite of that anticipated, and there was no association between FEV<sub>1</sub> and parental smoking. Home heating and FEV<sub>1</sub> residuals were also significantly associated at the 5 % level. The over-all means covered a 28-ml range and the ordering from low to high was oil, gas, electric.

Although FEV<sub>1</sub> residuals were affected by home heating fuels, the most consistent and significant finding was the lower levels of both FVC and FEV<sub>1</sub> in children whose homes had gas cooking stoves compared with those whose homes had electric stoves. The over-all effect of home cooking, after correcting for cohort effect, was 16 ml and 18 ml, respectively, for FEV<sub>1</sub> and FVC. This effect is apparent in almost all the cohorts. For FEV<sub>1</sub>, in 10 of 12 cohorts, the children in homes with gas stoves had lower function than children in homes with electric stoves (figure 4). For FVC, only 1 of the cohorts (St. Louis, first year), did not show lower levels of pulmonary function in children living in homes with gas stoves compared with those living in homes with electric stoves (figure 4). An unexpected finding in these data

was the low level of pulmonary function measured in Topeka, which is a city with generally lower levels of ambient pollution. In an attempt to investigate this finding, we tested the effect of different interviewers, we reread the spirometer tracings to test the effect of readers, and we compared the values obtained on each spirometer by month of study to test the possibility of a defective machine. None of these tests explained the lower pulmonary function values. In addition, the distribution of height for age of the children in Topeka did not differ significantly from the other cities. We were thus left with the observation that the pulmonary function measurements in the children in Topeka were lower than in other cities and must assume that it was a cohort effect needing further study.

#### Discussion

The significant associations found in this analysis were between home cooking stoves and both illness history and lung function. In addition, there was an association between parental smoking and disease history. The importance of these findings rests with the interpretations of these significant, albeit relatively small, changes. Sufficiently large groups are being studied to observe minor differences between them. The size of the differences found was consistent with the anticipated magni-

TABLE 3  
VALUES OF G<sup>2</sup> FOR SPECIFIED DISEASE RATES FOR EACH HOME VARIABLE  
AFTER ADJUSTING FOR THE OTHER TWO HOME VARIABLES

	Social Class		Parental Smoking		Home Cooking	
	G <sup>2</sup>	P	G <sup>2</sup>	P	G <sup>2</sup>	P
History of doctor-diagnosed bronchitis	0.70	NS	1.10	NS	1.90	NS
Serious respiratory illness before age 2	4.12	< .05	10.21	< .01	6.70	< .01
Respiratory illness in the last year	2.12	NS	4.38	< .05	0.14	NS

\* G<sup>2</sup> is a likelihood statistic derived from the log linear analyses and is distributed, in each case, like a chi square with 1 degree of freedom.

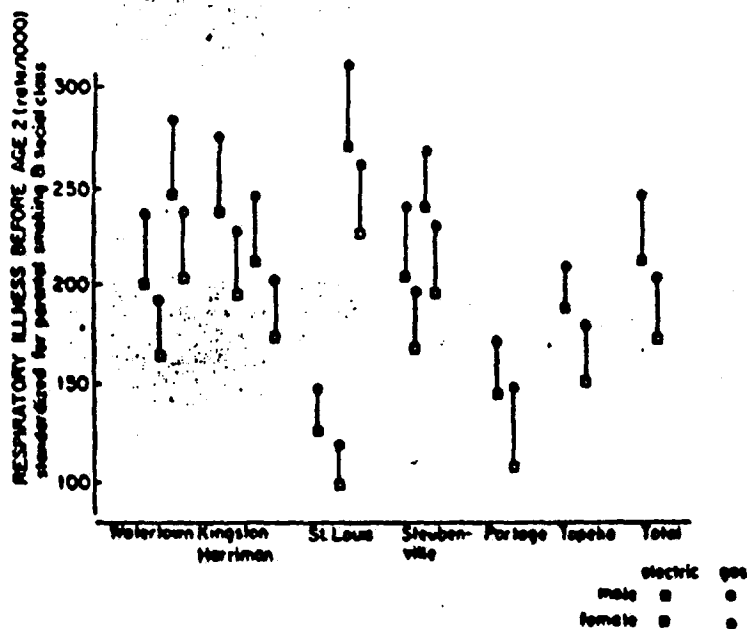


Fig. 3. Respiratory illness before age 2 standardized for parental smoking and social class by cohorts in children 6 to 10 yrs old. Males and females separately by cohort and gas or electric stoves.

tude of effect of environmental agents (11), and the home measurements of air quality are supportive.

The evidence that homes with gas cooking stoves have higher levels of  $\text{NO}_x$  than similar homes with electric stoves has been demonstrated a number of times (4, 5), and peak levels measured over gas stoves have on occasion been re-

ported to reach approximately 1 ppm ( $1,880 \mu\text{g}/\text{m}^3$ ) for periods of 10 to 15 min. This was confirmed in 1 household during continuous monitoring. Similarly we know from both our own investigation and from the studies of Hinds and associates (12) that the mass respirable particulate loads in households with smokers can be several-fold higher than in nonsmoking households.

TABLE 4  
ANALYSIS OF VARIANCE OF CHILDREN'S LUNG FUNCTION FOR HOME VARIABLES  
(CITY-COHORT ADJUSTED)\*

Home Variable	Children (no)	Lung Function Residuals			
		FEV, (liter)	F Ratio	FVC (liter)	F Ratio
Cooking fuel	6,803	—	—	—	—
gas	3,274	-.008	8.11†	-.009	7.94†
electric	3,529	+.008		+.009	
Home fuel	6,734	—	—	—	—
oil	1,419	-.011	3.26‡	-.005	0.78
gas	4,432	+.001		-.005	
electric	883	+.017		+.010	
Air conditioning	7,126	—	—	—	—
none	2,855	-.001	0.61	-.002	1.22
partial	2,363	+.003		+.006	
central	1,908	-.003		-.004	
Parental smoking	5,842	—	—	—	—
none	1,724	-.001	.03	-.011	6.28†
some	4,118	+.000		+.004	

\* See text for definition of different cohorts. Largest cohort home variable interaction terms gave F ratios of 1.3, not significant.

†  $p < .01$

‡  $p < .05$

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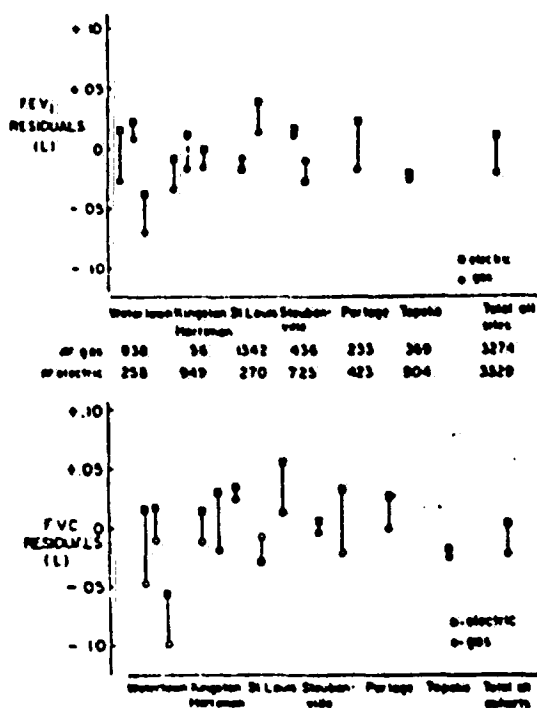


Fig. 4. Forced expiratory volume in 1 s and forced vital capacity residuals by cohort and gas and electric stoves in children 6 to 10 yrs old. (Numbers under the FEV<sub>1</sub> values are the same for FVC values.)

Other factors affecting the association between the disease and either the presence of gas stoves or smoking in the household seem to have been excluded (e.g., socio-economic status, presence of air conditioning, and the type of heating fuel).

In considering the importance of these findings, a number of potential sources of bias must be evaluated. The questionnaire information on disease rates for an individual child depends on the recall ability of the parents, and it may be biased by the present status of the child. The responses also may be biased by the parents' lack of knowledge. No attempt was made to have doctor confirmation of diagnosed disease confirmed independently. It seems unlikely, however, that any biases introduced by these means would be related to the type of home cooking stove consistently for each city and each cohort.

The good response rate, and the sampling plan that ensures that all potentially available children are seen means that the samples are representative of the cities.

The pulmonary function data are potentially subject to different sources of bias than the questionnaire data. These include possible interviewer bias, malfunctioning machine, and biased reading of the spirometer tracing. All these sources of bias have been looked for and have not been found. In

any case, neither the field screeners nor the readers were aware of the individual child's home environment when the spirometry was performed or when the tracings were read. Thus, we cannot attribute any bias to association with home variables.

Essentially, the interpretation of the pulmonary function finding relates to the sensitivity of the measurement and the biologic expectation of the magnitude of anticipated effect in a group of children between 6 yrs and 10 yrs of age. We used FEV<sub>1</sub> as a measure of air flow obstruction in these children, not because we believed it to be the best measure of early obstruction, but because our plan is to follow these children over several years. After several years they will be at a point at which a stable estimate of change in pulmonary function can be related to our understanding of the development of adult obstructive airways disease. In these children, many of whom can empty their entire FVC in less than 2 s, the FEV<sub>1</sub> does not measure obstruction as much as it measures FVC. Thus, it is reassuring to find similar changes in both measures when trying to understand the significance of any given finding.

Our understanding of the biology of lung growth and the nature of the onset of obstructive lung disease in adult life lead us to believe that only minor difference in the rate of functioning lung growth in young children could lead to these children not reaching their full adult lung size. (We are using FVC as a crude indicator of lung size recognizing that the TLC includes not only FVC but also the residual volume, which is not being measured in these field studies.) We do not know whether failure to reach full adult lung size is related to the subsequent susceptibility of developing obstructive lung disease, but it is not an untenable hypothesis that those persons with minor impairment of total lung growth are more susceptible to rapid decline in pulmonary function in adult life (13).

These results differed from those reported in the literature to date only in modest ways. The findings of Mehta and co-workers (2) regarding lower respiratory tract illness rates in children whose homes have gas stoves were similar. That study was criticized because it did not have smoking data. In this study the adjustment of rates of illness before age 2 for smoking led to a clear association with gas cooking devices; however, the adjustment of the other 2 historical disease indicators reduced the associations found. The study of Keller and associates (14) of both adults and children in a selected sample of households suggest no association of gas stoves with respira-

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tory disease rates. This study measured incidence of acute respiratory disease over the course of 1 year; but the number of children studied was quite small and clearly did not represent a general population. Bouhuys and co-workers (15) did study population-based samples of children and adults, but out of the 7,000 persons studied only 165 children between the ages of 7 yrs and 14 yrs were included from the 2 communities under investigation (16). Thus, the fact that they were unable to find an association with home cooking devices may be attributed to the small number studied.

Tager and associates (17), using a different indicator of airways obstruction (mid-maximum expiratory flow), found an association between the pulmonary function levels in children and the number of smokers in the household. No such association using FEV<sub>1</sub> was found in this study. This may mean that the airways obstruction measurement was insensitive.

Further follow-up of these cohorts are underway. Because these data deal with retrospective information, the initial findings reported here need replication to ensure that some subtle bias or alternative explanation for the findings has not been overlooked. If the relative position of these children's lung sizes changes on repeated assessment, it will be important to assess the factors that influence the change. These factors may include changes in ambient pollution (outdoor levels) or changes in personal pollution (indoor exposures and cigarette smoking). In addition, other personal factors such as frequency of respiratory infections, familial history of disease, or other recognized potential risk factors for developing chronic obstructive respiratory disease not discussed in this report will need to be considered.

#### Acknowledgment

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Lebowitz, M.D., Armet, D.B., Knudson, R. "The Effect Of Passive Smoking On Pulmonary Function In Children" Environment International 8: 371-373, 1982.

The authors of this study conducted an investigation of ventilatory function in 344 nuclear families in a representative population sample in Tucson, Arizona. Household aggregation of body mass was investigated as a possible confounding factor in the reported association between impaired lung function and parental smoking. The authors report that "when household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking." The study concludes with the statement that "[i]t must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function."

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## THE EFFECT OF PASSIVE SMOKING ON PULMONARY FUNCTION IN CHILDREN

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A study of ventilatory function was conducted in 344 nuclear families in a representative community population sample in Tucson, AZ. Household aggregation of pulmonary function, which is dependent on household aggregation of body mass, might affect the relationship of children's pulmonary function to parental smoking. When household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking. The trend, in the opposite direction, was similar to that found by Speizer *et al.* (1980a), but was not significant in this study. It must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function.

### Introduction

There has been some controversy surrounding the issue of whether passive smoking in households effects the respiratory health of children (NRC, 1981). Some investigators have reported that childhood symptom rates appear related to parental smoking, whereas others disagree. However, it is better to utilize pulmonary function to determine this effect, inasmuch as symptom reporting may show tendencies for parental biases (Cederlof and Colley, 1974; Lebowitz and Burrows, 1976; Schilling *et al.*, 1977). One study by Tager *et al.* (1979) showed the effect of parental smoking on FEV<sub>1</sub>, utilizing Z scores. A similar analysis from the same laboratory in six other, different populations (Speizer *et al.*, 1980a) showed opposite results. Tager *et al.* (1976) also showed that there was household aggregation of pulmonary function values, which might influence such a relationship. This study has demonstrated the relationship of active smoking to ventilatory impairment (Knudson *et al.*, 1976; Burrows *et al.*, 1977), as has been found by others.

This paper attempts to examine the effects of parental smoking on children's pulmonary flow and volumes after correcting for any familial aggregation of ventilatory function and body size.

### Methods

The Tucson Epidemiological Study of Airways Obstructive Diseases, which provided the data base for

these analyses, has been described previously (Lebowitz *et al.*, 1975). Briefly, it is a multistage stratified cluster sample of white non-Mexican-Americans in the Tucson area, where stratification was on age of head of household and on social status. Of the 1655 families studied (approximately 3800 individuals), families with children biologically related to the parents were chosen; these represented 344 households and about one-half of the population (1400). In the first year of this study (1972-1973), pulmonary function tests had been satisfactorily completed on over 90% of those age 6 and over using techniques previously described (Knudson *et al.*, 1976). Smoking habits in adults have been described previously (Burrows *et al.*, 1977); they are similar to those found elsewhere and cover the whole range of amount and duration of smoking.

These nuclear families were divided also into parent-child, spouse, and sibling pairs, the former using oldest children, by sex. Z scores [standard normal deviates  $Z_i = (x_i - \bar{x})/s$ , for  $i$  individuals and  $j$  age-sex groups] were calculated for forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), maximum flow at 50% of the vital capacity ( $V_{50}$ ), and maximum flow at 75% of the expired vital capacity ( $V_{75}$ ), within each sex-age group represented in the parent-child pairs. The Z scores were used in analyses of variance to correct for genetic components of body mass in pulmonary function parameters and to detect relationships between parental smoking and children's pulmonary function.

Most houses in this study, as determined by survey, are 1800–2400 ft<sup>2</sup>, not more than 20 years old, have typical 8 ft ceilings, have screened windows, and have central heating and air cooling (usually with filters for both systems). They are kept relatively closed in summer and winter, but are somewhat more open in spring and fall. Air exchange rates have not been measured in this study, but are estimated using published information (NRC, 1981) at between 0.4 and 2.0 per hour, depending on season and use of forced air systems. Indoor pollutant levels were not measured in all of these houses as part of this study. Infiltration of suspended particulate has been measured in about 41 houses (Lebowitz *et al.*, 1982) and is low, though indoor generations is not. Carbon monoxide (CO) indoors and out has been also measured (Lebowitz *et al.*, 1982) and are low as well. The use of types of stoves has been measured in only some families (Lebowitz *et al.*, 1982). Outdoor levels of particulate alone are high in this area, but it is a silica quartz particulate. Nitrogen dioxide and CO are variable, but not in excess of NAAQS (Pima County, 1981).

## Results

It was found that there was a household aggregation of pulmonary function values and of body size. Body size is the key determinant of ventilatory function values (Knudson *et al.*, 1976). When the household aggregation of body size was corrected, there was no household aggregation of pulmonary function that was still significant. Therefore, all pulmonary function values were expressed as percent predicted where the children's prediction equations use their own body size values, their age, and the body size values of their parents. Body size values used included height, weight, sitting height, and the ponderal index (H/W 1/3). Parents' pulmonary

function values were expressed as percent predicted, where the prediction equations used their body size values and their ages. Z scores were then calculated from these percent-predicted values for the age and sex groups (see above).

Analyses of parent-child, spouse, and sibling pairs by the smoking habits of the family members did not show any significant correlations of passive smoking with pulmonary function. This was true whether children's smoking or not smoking was accounted for, and was also true regardless of whether the parents had airway obstructive disease or abnormal pulmonary function tests. It was also independent of family size. Analyses of variance were performed for the children's pulmonary function test values by smoking in the household, by whether both parents smoked, or whether the mother smoked, father smoked, or neither. The total number of nuclear families was reduced to 271 when both parents and all the children age 6 and over in the household had satisfactory pulmonary function data. As can be seen in Table 1, none of the results were statistically significant. Analysis by amount of parental smoking yielded similar results.

In subsequent years of this study, further symptom information and history was collected. Analysis of these data in relation to passive smoking, using previous methods (Lebowitz and Burrows, 1976), indicated no relation to present or past symptoms, including persistent wheeze or early childhood lower respiratory tract illness. Further analysis awaits collection of more longitudinal ventilatory function measurements on the children.

## Discussion

The effects of similar pollutants (specifically NO<sub>2</sub>, CO) from the use of gas stoves on children's and adults'

Table 1. Children's pulmonary function by parental smoking in nuclear families.

Parental Smoking	n	FEV <sub>1</sub> (Z-score) <sup>a</sup>		FVC (Z-score)	
		Mean	SD <sup>b</sup>	Mean	SD
Neither smokes	48	-0.121	0.993	-0.082	0.997
Mother smokes	35	-0.157	0.812	-0.157	0.925
Father smokes	92	-0.042	0.970	-0.059	0.913
Both smoke	96	+0.232	1.059	+0.186	1.062
Total	271	0.026	0.996	0.011	0.988
ANOVA:		p = 0.0796		p = 0.1798	
		V <sub>max</sub> 50% (Z-score)		V <sub>max</sub> 75% (Z-score)	
		Mean	SD	Mean	SD
Neither smokes	48	-0.160	1.194	-0.075	1.058
Mother smokes	35	-0.147	0.848	+0.004	0.888
Father smokes	92	-0.174	0.945	-0.173	1.011
Both smoke	96	+0.150	0.985	+0.202	0.972
Total	271	-0.0002	0.998	-0.0001	0.998
ANOVA:		p = 0.2443		p = 0.072	

<sup>a</sup>See text for explanation.

<sup>b</sup>SD = standard deviation.

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symptoms and pulmonary function were explored separately, inasmuch as previous studies indicate such potential effects (Speizer *et al.*, 1980b; Comstock *et al.*, 1981). In a substudy, gas stove use was related to acute symptoms only. Analysis in relation to chronic lung disease and ventilatory function had been performed on the total population of 1655 families; gas stove usage was not related to these measures of disease (Lebowitz, 1977). In that same study, it was shown that ambient outdoor particulate matter was slightly related to those measures of disease, but household size and type of house were not (after controlling for socioeconomic status). Socioeconomic status has little independent contribution to pulmonary function (or disease) once more important factors are considered, such as active smoking (Lebowitz, 1982). Thus, these other factors were not part of the analyses reported herein.

It is possible that correction for family body size concordance is not always necessary (Schilling *et al.*, 1977; Speizer *et al.*, 1980a, 1980b). The presence of persistent symptoms, such as wheeze, may be important in some populations (Weiss *et al.*, 1980), but were not in this population. However, consideration of fuel used for heating and cooking is necessary, especially when passive smoke appears important (Speizer *et al.*, 1980a, 1980b; Comstock *et al.*, 1981; NRC, 1981). Results, especially in lower socioeconomic classes or in developing countries, could be misleading otherwise. On the other hand, there still may be an effect of passive smoking, even when accounting for other exposures, in some circumstances and/or some communities, dependent on environmental circumstances, home ventilation factors, and social class.

A more extensive discussion of these factors and their interactions can be found in the National Research Council report (1981) and in an editorial by Frank and Lebowitz (1981).

**Acknowledgement**—This work was supported by NHLBI SCOR Grant No. HL14136.

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National Institutes of Health, "Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiological Studies", December 1983, pp. 1-11.

**SUMMARY:** The 1979 Surgeon General's Report on smoking and health presented the available scientific evidence that links involuntary cigarette smoke exposure (passive smoking) to adverse health effects. Existing evidence suggests that children of parents who smoke have more bronchitis and pneumonia during the first year of life and that acute respiratory disease accounts for a higher number of restricted activity days and bed disability days in children whose families smoked than in those whose families did not. In adults, small airway function impairment equivalent to that observed in light smokers has been reported in adults who had never smoked or, lived with smokers but were only exposed to cigarette smoke in the work place. Results such as these need to be confirmed and validated. A number of studies involving large population groups are presently addressing the question of the effect of passive smoking on the respiratory system. However, these studies which are being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions.

An important goal of this workshop was to provide a common forum to these different groups of investigators, along with statisticians conversant with this area, so that the various study designs and results obtained so far could be reviewed in order to identify the probable reasons for differences. Other goals of the workshop were to develop guidelines for collection and analysis of epidemiologic data on the respiratory effects of passive smoking, and to make recommendations for future studies.

The participants included epidemiologists involved in three ongoing population studies of the effect of passive smoking on respiratory health, statisticians, and adult and pediatric pulmonary physicians. The presentations (see Appendix A for agenda) dealt with data from the three groups and methodologic issues relating to data collection and statistical analysis, as well as results of other relevant studies carried out both in the US and other countries. After the first day of formal presentations, the workshop participants (see Appendix B for the list of participants) were divided into smaller task groups, each of which addressed the issues of measuring smoke exposure, outcome variables, confounding variables, other statistical issues related to design and analysis, and the need for additional studies. The following is a summary of the presentations, discussions and recommendations of the task groups.

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REPORT OF WORKSHOP  
ON  
RESPIRATORY EFFECTS OF INVOLUNTARY  
SMOKE EXPOSURE: EPIDEMIOLOGIC STUDIES

May 1-3, 1983

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service  
National Institutes of Health

December 1983

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### FOREWORD

On May 1-3, 1983, the Division of Lung Diseases, National Heart, Lung, and Blood Institute sponsored a Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, which was held in Bethesda, Maryland. Twenty-one investigators from the fields of epidemiology, statistics, and adult and pediatric pulmonary medicine participated. This report, prepared by the workshop chairman, session recorders, and Division of Lung Diseases staff, summarizes the presentations and makes recommendations for future studies.

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## TABLE OF CONTENTS

	<u>Page</u>
I. INTRODUCTION . . . . .	1
II. COMMUNITY-BASED STUDIES ON THE PULMONARY EFFECTS . OF PASSIVE SMOKING . . . . .	2
III. METHODOLOGIC CONSIDERATIONS. . . . .	2
IV. CONCLUSIONS OF WORKING GROUPS. . . . .	4
V. RESEARCH RECOMMENDATIONS . . . . .	6
VI. SUMMARY AND CONCLUSIONS. . . . .	7
VII. APPENDICES	
A. AGENDA . . . . .	8
B. PARTICIPANTS. . . . .	10

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## INTRODUCTION

The 1979 Surgeon General's Report on smoking and health presented the available scientific evidence that links involuntary cigarette smoke exposure (passive smoking) to adverse health effects. Existing evidence suggests that children of parents who smoke have more bronchitis and pneumonia during the first year of life and that acute respiratory disease accounts for a higher number of restricted activity days and bed disability days in children whose families smoked than in those whose families did not. In adults, small airway function impairment equivalent to that observed in light smokers has been reported in adults who had never smoked or, lived with smokers but were only exposed to cigarette smoke in the work place. Results such as these need to be confirmed and validated. A number of studies involving large population groups are presently addressing the question of the effect of passive smoking on the respiratory system. However, these studies which are being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions.

An important goal of this workshop was to provide a common forum to these different groups of investigators, along with statisticians conversant with this area, so that the various study designs and results obtained so far could be reviewed in order to identify the probable reasons for differences. Other goals of the workshop were to develop guidelines for collection and analysis of epidemiologic data on the respiratory effects of passive smoking, and to make recommendations for future studies.

The participants included epidemiologists involved in three ongoing population studies of the effect of passive smoking on respiratory health, statisticians, and adult and pediatric pulmonary physicians. The presentations (see Appendix A for agenda) dealt with data from the three groups and methodologic issues relating to data collection and statistical analysis, as well as results of other relevant studies carried out both in the US and other countries. After the first day of formal presentations, the workshop participants (see Appendix B for the list of participants) were divided into smaller task groups, each of which addressed the issues of measuring smoke exposure, outcome variables, confounding variables, other statistical issues related to design and analysis, and the need for additional studies. The following is a summary of the presentations, discussions and recommendations of the task groups.

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## COMMUNITY-BASED STUDIES ON THE PULMONARY EFFECTS OF PASSIVE SMOKING

Findings from community studies of the effect of passive smoking on the respiratory system were summarized. These presentations included data from populations in East Boston, Massachusetts, the Six Cities Study, Tucson, Arizona, and Tecumseh, Michigan. Although none of these studies were originally designed to address the question of the effect of passive smoking on the respiratory system, all have succeeded in obtaining a considerable amount of relevant data.

The methods of data collection and data analysis are somewhat different from group to group, and the results and conclusions of the studies also showed differences. All of the studies have been using questionnaires to assess exposure and symptom prevalence and, in general, the one second forced expiratory volume ( $FEV_1$ ) has been used as the lung function outcome variable of interest.

Most of the available data that have been analyzed are cross-sectional in nature; longitudinal data from a cohort followed for seven years in East Boston, Massachusetts, have been published since the workshop. In the cross-sectional community-based population studies, the effect of passive smoking on lung function varied from none to a very small effect (0 - 3% loss in  $FEV_1$ ). In the longitudinal study, a measurable effect on the development of pulmonary function was seen in the children with a mother who smoked throughout the child's life. Whether this reflects a postnatal effect of passive smoking on lung growth and development, an in utero effect or an effect on bronchial reactivity such that some individuals exposed to passive smoking develop an increase in bronchial reactivity, an increase in mucus in the airways, increased susceptibility to lower respiratory tract infection or some other as yet undefined effect is not yet clear. Better measures of exposure, more longitudinal data and more information about bronchial reactivity are needed before this can be resolved. Better measures of exposure will probably involve biological monitoring, for example, the measurement of cotinine in biological fluids such as saliva and urine. The size and complexity of the data sets accumulated in these population based studies have necessitated the development of new analytical techniques and the adaptation of existing techniques to apply to both cross-sectional and longitudinal data.

## METHODOLOGIC CONSIDERATIONS

The relatively small differences in the effects found in the various studies discussed at this workshop may be real and represent true differences among the various communities studied in the measurable effect of involuntary smoke exposure. Such differences may be caused by regional and geographic

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variations in levels of indoor air pollution that might result from differences in housing - (e.g., well insulated versus poorly insulated houses,) and life style (e.g., predominantly indoor living versus predominantly outdoor living.) On the other hand, the differences may also be due to methodologic differences in data collection and/or analysis and in the way in which potentially confounding variables have been handled.

The difficulty of controlling for potentially confounding variables was recognized. Such variables include: 1) unvented combustion products from different kinds of stoves used for both heating and cooking, e.g., gas, wood and kerosene, 2) other indoor pollutants such as formaldehyde and respirable particulate matter, 3) indoor pollutants of organic origin such as pollens, molds, mites, other allergens and infectious organisms, 4) characteristics of indoor environments such as temperature, humidity, and frequency of air exchanges, 5) socio-economic status, culture (ethnic), and such factors as crowding, number of siblings, household conditions, child care, reporting biases, etc., 6) demographic and medical characteristics of the study population such as age, sex, marital status, the presence of underlying respiratory conditions, atopy, infections, disability and/or co-morbidity, 7) parental symptoms such as productive cough which will affect reporting, 8) maternal smoking during pregnancy, 9) annoyance responses and other psychological or social responses to tobacco smoking in a nonsmoker. Extensive as this list of potentially compounding variables may be, the importance of taking them into consideration in the study design and analysis cannot be overemphasized.

Given the complexity and number of the potentially confounding variables, the importance of analyzing all the data sets using a common statistical approach was recognized. Also, the importance of distinguishing a statistically significant difference between groups from a clinically significant difference was emphasized. In this regard, a small difference (e.g., 1-3% in  $FEV_1$ ) in a cross-sectional study between children from homes in which one parent smoked and those from homes in which no one smoked, might be statistically significant but not be of any clinical significance. On the other hand, a 7% difference in rate of increase in  $FEV_1$  over 7 years observed longitudinally may be both statistically and clinically significant. It is therefore important to use outcome variables (such as  $FEV_1$ ) which are of clinical importance rather than using other lung function tests which are extremely sensitive. Likewise, longitudinal data are generally more useful and informative than cross-sectional data.

Many of the differences among the many population studies which have looked at the effect of active and passive smoking on the lung function may be attributable to exposure and/or dose. The logistical difficulties in adequately monitoring these variables are recognized as is the need to develop techniques which are able to measure the biological burden of tobacco smoke. In the future it is likely that considerably less attention will be paid to indirect measures of exposure such as area and personal samplers and more attention paid to biological markers of exposure.

#### IV

### CONCLUSIONS OF WORKING GROUPS

#### A. Study populations

None of the population studies already under way was designed specifically to look at the effect of passive smoking on the respiratory system. However, if the results from these studies show consistency, it may be possible to arrive at answers to most of the questions about the effects of passive smoking on the lungs. Existing data sets should be analyzed and the results compared before any further studies are designed to address this question. An exception to this might be for the age group 0-5 years for which there is very little existing information or planned study because of the difficulties inherent in obtaining accurate measures of lung function in this age group. Also of particular interest are the changes taking place in lung function during the transition between the late teen years and early twenties and the decline in lung function in early adult life. There is presently insufficient information about the possible effect of risk factors such as passive smoking on this transition phase. Another area of particular interest is the occupational setting. It may be that passive smoking is more hazardous in certain occupational settings than in others.

#### B. Outcome Variables

The usual measures of outcome that are presently employed are 1) some measure of lung function and 2) questionnaire information. Every attempt should be made to obtain information in a standardized fashion, (as is presently being done in most of the ongoing studies). Since there are differences of opinion as to which measure of volume or flow should be regarded as the "best" measurement, it is recommended that the complete flow-volume or volume-time curves should be saved. In addition, more attention should be paid to obtaining information about airway reactivity since the existing evidence suggests that exposure to passive smoking may alter an individual's airway reactivity. Also, there is an urgent need to develop pulmonary function tests for use in very young children (below five years), with particular attention to linking these tests with those for older age groups.

Most groups are presently using the standardized ATS-DLD respiratory symptom questionnaire to define symptoms and disease states. It should be noted that this questionnaire was developed to define disease states such as chronic bronchitis and, therefore, may not be entirely suitable to elicit the symptoms associated with passive smoking. Likewise, the pediatric questionnaire was not developed with the idea of identifying symptoms associated with passive smoking. It is recommended, therefore, that new questions should be designed to add to both the adult and the pediatric question-

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naires to obtain information, in a standardized fashion, about involuntary smoke exposure.

C. Measurement of Dose/Exposure

Lack of proper attention to the estimation or measurement of exposure is a major weakness of all the studies carried out so far. Direct measurement of exposure to tobacco smoke and other combustion products is, at present, too difficult to consider in population studies. It is possible, however, to significantly improve our estimates of exposure. This can be done by developing standardized questions for characterization of indoor sources of pollution, including smoking and by using passive monitors to estimate average ventilation within buildings. Probably most important is the evaluation of biological monitors, in particular, urinary and salivary cotinine levels as indicators of levels of exposure to tobacco smoke.

D. Confounding Variables

There are many potential confounding variables which must be taken into account. Data on these variables are not presently being collected uniformly among the studies underway. It is hard to recommend any specific strategy with regard to confounders, but it must be emphasized that any study which ignores them will be seriously flawed. A list of potentially confounding variables is provided in Section III.

Atopy is important to measure, but cannot be determined by questionnaire data. Only skin tests and IgE measurements are appropriate at present. The development of a standardized approach to measuring the atopic status of an individual should be undertaken.

E. Other statistical issues in design and analysis

The investigators agreed that the various study groups should attempt to cross validate results using analytic techniques from other studies on their own data. Existing statistical methods plus the adaptations of existing methods that have been developed provide a good starting place. In certain instances new methods will still need to be developed. For each study and data set, it is important to place confidence limits on the results, evaluate them in the light of possible biases specific to that study and interpret the results in terms of whether they are clinically and biologically meaningful as well as statistically significant.

F. Additional studies

The participants concluded that the existing studies and data sets should be explored extensively and the results of the various studies compared in order to see if an agreement on the effect of passive smoking on the respiratory system may be reached by the various investigators. Following such an analysis, it will probably be clear as to whether new studies need to be designed to answer specific questions.

It may also be worthwhile to explore other existing data sets which may have obtained information about exposure to passive smoking such as MRFIT, Framingham, the UK National Birthday study (1952), the Japanese (Hirayama) data set and French (Kauffman) data sets.

One area that does need additional study is the development and testing of better measures of involuntary smoke exposure, such as area and personal air samplers and biological markers of exposure. For example, salivary and urinary cotinine levels. These need to be non-invasive.

## V

### RESEARCH RECOMMENDATIONS

#### A. Available data

1. The groups with ongoing studies should be encouraged to use common methods of analysis in addition to any methods they are already employing.
2. The use of standardized methods for obtaining questionnaire and lung function data should be continued. However, questionnaires specifically designed to define disease or symptoms in smokers may not be adequate and new questions capable of eliciting more subtle responses are needed.
3. Where possible, a measure of bronchial reactivity and a measure of an individual's atopic status using skin tests and serum IgE should be included.
4. All possible confounding variables need to be taken into account in any analyses.
5. Measures of exposure such as salivary and urinary cotinine ought to be obtained to validate questionnaire results.

#### B. New Studies

1. Additional studies are probably required in young children (below five years) to obtain more information about the relationship between passive exposure to tobacco smoke and the incidence of lower respiratory tract infections, the development of symptoms, lung growth and lung function.
2. Improved methods of measuring exposure to both tobacco smoke and other indoor pollutants need to be developed and validated. An example of this is the use of salivary and urinary cotinine.

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## SUMMARY AND CONCLUSIONS

A review of the data from the studies which have been carried out or are in progress which address the effect of passive smoking on the respiratory system suggests that the effect varies from negligible to quite small. From this review, it was not possible to determine whether there is a specific group which is at increased risk or what the mechanism of the effect (if any) may be. The data sets which already exist and are presently being collected are large and complex and, not surprisingly, there are differences, although small, in the results, among the data sets discussed at this workshop. These differences may be due to real differences among the populations being studied or may be due to methodologic differences that inevitably occur from study to study, both in the data collection and analysis. A common approach to the analysis may help to answer this question. It seems likely that the existing data sets contain sufficient information to allow some conclusions to be reached on the effect of passive smoking on the respiratory system. New large scale population studies (of subjects above 5 years of age) should probably not be initiated until the existing data sets have been thoroughly evaluated. There is, however, an urgent need for the development and evaluation of non-invasive biological markers of exposure.

APPENDIX A

DIVISION OF LUNG DISEASES

WORKSHOP ON RESPIRATORY EFFECTS OF INVOLUNTARY SMOKE EXPOSURE:  
EPIDEMIOLOGIC STUDIES

May 1-3, 1983

Chairman: Sonia Buist

May 1

Welcome

Smoking and Pulmonary Health - Goals of Workshop

Pulmonary Effects of Passive Smoking

S. Hurd

S. Buist

C. Rossiter

May 2

COMMUNITY BASED STUDIES ON THE PULMONARY EFFECTS OF  
PASSIVE SMOKING

Moderator: S. Buist

Studies from Boston, Massachusetts

I. Tager

F. Speizer

S. Weiss

D. Dockery

B. Ferris

B. Rosner

T. Louis

Studies from Tucson, Arizona

B. Burrows

M. Lebowitz

L. Taussig

Studies from Ann Arbor, Michigan

M. Higgins

I. Higgins

J. Keller

A. Monto

OTHER STUDIES AND METHODOLOGICAL ISSUES

Moderator: H. Weill

WHO Studies

M. Lebowitz

Measurement of Indoor Pollution

J. Stolwijk

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May 3

GROUP DISCUSSIONS TO DEVELOP RECOMMENDATIONS  
ON THE FOLLOWING ISSUES

Exposure Measures

Outcome Variables

Confounding Variables

Other Statistical Issues in Design  
and Analysis

Additional Studies

FINAL PRESENTATIONS AND RECOMMENDATIONS

Moderator: S. Buist

SUMMARIES OF GROUP DISCUSSIONS

RECOMMENDATIONS FOR FUTURE RESEARCH

CONCLUDING REMARKS

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## APPENDIX B

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"Relationship of Parental Smoking and Gas Cooking to Respiratory  
Disease in Children" Chest 64: 662-668, 1983.

SUMMARY: In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home ( $p < 0.001$ ) or at least one of the parents smoked ( $p < 0.02$ ). The occurrence of cough with colds in children was also significantly increased when one or both parents smoked ( $p < 0.001$ ). Small but significant increases ( $p < .05$ ) in the mean values of forced expiratory volume at one second, the flow rate of 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF 25-75) were seen after administering inhaled isoproterenol to children whose parents smoked ( $n = 94$ ) but not among children whose parents did not smoke ( $n = 89$ ); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six - to 12-year-old children with no other history of chronic respiratory illness.

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# Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children\*

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In a survey of 1,353 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home ( $p < 0.001$ ) or at least one of the parents smoked ( $p < 0.02$ ). The occurrence of cough with colds in children also was significantly increased when one or both parents smoked ( $p < 0.001$ ). Small but significant increases ( $p < .05$ ) in the mean values of forced expiratory volume at one second, the flow rate at 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF<sub>25-75</sub>) were

seen after administering inhaled isoproterenol to children whose parents smoked ( $n = 94$ ) but not among children whose parents did not smoke ( $n = 89$ ); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six- to 12-year-old children with no other history of chronic respiratory illness.

Parental smoking has been shown to be related to increased risk of respiratory illness in children during the first year of life,<sup>1,2</sup> and to an increased risk of morning cough, respiratory infections, and breathlessness among older children.<sup>3,4</sup> Specifically, an increased incidence of pneumonia and bronchitis with consequent hospitalizations has been reported among infants whose parents smoked compared to children whose parents did not smoke.<sup>1</sup> Parental smoking also

the relationship of parental smoking and gas cooking on the occurrence of respiratory illness and symptoms in children from a midwestern university community. Additionally, we examined the relationship between these environmental exposures and pulmonary functions.

## METHODS

### Subjects

Children, ages 6 to 12, who attended primary school in the Iowa City School District were contacted after permission was obtained from school administrators. The school district serves a university community. The children were therefore generally from middle and upper social classes. Participating schools included approximately 87 percent of the 2,062 children six to 12 years of age enrolled in the school district. Children from the participating schools were sent home with a letter explaining to parents the purpose of the studies, the information we were interested in collecting and why. The parents were requested to complete a modification of the questionnaire developed by the American Thoracic Society (ATS) for the Division of Lung Disease (DLD) of the National Heart, Lung, and Blood Institute (the ATS-DLD questionnaire)<sup>5</sup> and to return it to us in a stamped, self-addressed envelope. (A copy of the modified questionnaire is available on request from the authors.) Two weeks following the initial distribution of the questionnaires to the parents, another letter was sent as a reminder to parents who had failed to return a completed questionnaire.

In order to determine if nonrespondent parents and their children differed significantly in certain characteristics from those parents who had completed the questionnaire about their children, 200 nonrespondent parents were randomly selected and contacted by telephone by a trained research assistant four weeks after the questionnaires were initially sent to the parents. The parents were each read the part of the questionnaire that related most directly to cigarette smoking and respiratory illness. To ensure that the questions were answered accurately, these pertinent questions from the questionnaire were read aloud exactly as printed and without any elaboration by the research assistant.

### Pulmonary Function Measurements

Pulmonary function measurements were obtained from 89 chil-

For editorial comment see page 651

has been reported to increase the risk of persistent wheeze<sup>6</sup> and symptomatic asthma.<sup>7,8</sup> In a study of British secondary schoolchildren that showed early morning cough to be more commonly reported by children who smoked, the effect on these smoking children of parental smoking appeared to be additive.<sup>4</sup> A decrease in pulmonary function measurements also has been noted in nonsmoking children whose parents smoked.<sup>9,10</sup>

An association has been similarly shown between respiratory illness in children and gas cooking, apparently from increased levels of nitrogen dioxide and nitric oxide in the homes with gas stoves.<sup>11,12</sup> In addition, pulmonary function measurements performed in school age children were found to be lower in association with the use of gas stoves in the home.<sup>13,14</sup>

The current study was designed to further examine

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children (47 girls and 41 boys) whose parents did not smoke and 94 children (52 girls and 42 boys) whose parents smoked. These children were randomly selected using tables of random numbers from the children for whom complete information was obtained using the questionnaire. All parents were requested to indicate their consent for pulmonary function studies to be obtained from their children, after we had provided a full written explanation of the reasons for obtaining the measurements and the procedures the child would follow during pulmonary function testing. Consent was obtained from 411 (85.6 percent) of the 484 children whose parents did not smoke and 596 (91.1 percent) of the 654 children whose parents smoked. When parental smoking was kept constant, the proportions of children who had cough with cold, cough apart from colds, or phlegm with or apart from colds were not significantly different for consenting parents compared to nonconsenting parents. We therefore felt that our sampling procedure produced a representative population of children.

Children were excluded if there was a history of recurrent respiratory illness or if there was any history of upper or lower respiratory infection during the prior six months. Spirometry was measured with a Jones Pulmonary waterless respirometer. Calculations of the parameters measured were done by the Jones Datamatic Computer with daily calibration. Lung volumes were measured by use of a plethysmograph (model 2000B, Collinspulmonary Instruments) using a 3 L-second Fleisch temperature-controlled pneumotach, with a flow accuracy of  $\pm 1$  percent of full scale.

Each child was instructed in the measurement maneuver and was in an upright sitting position. Each test was repeated three to five times, and the best effort was taken. Flow rates and lung volumes were measured before and five minutes subsequent to 1.25 mg inhaled isoproterenol diluted with 2 ml normal saline solution and administered by an open nebulizer.

#### Analysis of Data

Discrete multivariate analysis was used to study the interactions among factors.<sup>22</sup> In this analysis, maternal and paternal smoking and gas cooking were treated as independent factors, while the frequencies of various respiratory symptoms or illness were the dependent variables. The reported prevalence of respiratory symptoms or illnesses were stratified by parental smoking (mother alone, father alone, both parents, either or both parents, neither parent smokes) and by cooking fuel use. Odds ratio was calculated for each interaction effect. Odds ratios greater than one indicated that the variable had a higher risk for the children and conversely odds ratios of less than one indicated lower risk. A chi-square analysis was used to examine the significance of the odds ratio.

Regression lines were fitted to each of the pulmonary function measurements using the Statistical Analysis System (SAS) using the stepwise procedure.<sup>23</sup> The variables entered in the equation were

age in years, sex, weight (kg), and standing height (cm). Lines were fitted separately for children from smoking and nonsmoking environments, as well as for values obtained by pooling these two groups. F-tests were performed as described by "Neter and Wasserman"<sup>24</sup> to compare the fit of the lines obtained for values for children from the two environments and for the pooled data. Paired t-tests were used to compare the prebronchodilator and postbronchodilator pulmonary functions.

#### RESULTS

Completed questionnaires were obtained for 1,355 children, or 65.7 percent of the children six to 12 years of age in the school district. Of the 1,355 completed questionnaires, data on parental smoking history was complete for 1,138 (84 percent) of the children. In the remaining 217 questionnaires, either maternal or paternal or both smoking histories were unrecorded or incompletely recorded. The proportion of children with incomplete or no parental smoking history who had cough with or apart from colds, congestion or bringing up phlegm, or had chronic lung diseases was not statistically significantly different from the proportion of children with parental smoking histories who had these symptoms. These questionnaires were eliminated in subsequent analysis. Forty-nine percent of these children were males, and 51 percent were females. Five percent of the children had established diagnoses of chronic respiratory diseases. Two had cystic fibrosis, one had pulmonary tuberculosis, two had diagnoses of chronic bronchitis, and 49 had asthma. When we compared the 200 randomly selected nonrespondent families to our study population, we found no statistically significant differences in the proportion of parents who smoked at home. The proportions of children who had cough with colds, cough apart from colds, or who had congestion or bringing up phlegm with or apart from colds were not significantly different among the two groups.

Fifteen percent of the parents completing the questionnaire indicated they had bronchitis, emphysema, asthma, or other chronic respiratory condition. We found no relationship between the report of chronic respiratory illnesses in parents and the reported prevalence in children of symptoms of cough with colds,

Table 1—Proportion of Children with Cough with Colds or Hospitalized for Chest Problems Before Age 2 Years, by History of Parental Smoking and Home Cooking Fuel Used

Home Cooking Fuel	Parental Smoking History (Yes = Parent Smokes)		Percentage of Children Affected (Total Number of Children in the Group)	
	Father	Mother	Cough With Colds	Hospitalization For Chest Illnesses
Gas	No	No	32.8 (137)	5.1 (138)
Gas	No	Yes	35.7 (28)	7.1 (28)
Gas	Yes	No	35.6 (101)	8.0 (100)
Gas	Yes	Yes	30.6 (111)	9.8 (112)
Electricity	No	No	28.9 (343)	2.1 (34)
Electricity	No	Yes	37.7 (69)	8.8 (68)
Electricity	Yes	No	37.7 (69)	5.6 (178)
Electricity	Yes	Yes	44.5 (17)	1.2 (172)

Table 2—Association of Parental Smoking and Gas Cooking with Hospitalization of Children Before Age 2 Years for Respiratory Illnesses

Independent Variables	No. of Children Hospitalized for Chest Illnesses		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	28	350	2.4	0.684	0.001
Electricity	25	736	1.0	...	...
Parental smoking					
Father alone smokes	18	360	2.3	0.856	0.022
Mother alone smokes	8	90	2.9	1.279	0.026
Father and mother smoke	13	371	1.6	0.856	0.21
Either or both parents smoke	39	621	2.1	0.666	0.017
Neither parent smokes	14	465	1.0	...	...

enough apart from cold, or bringing of phlegm with or apart from colds. Of the 1,138 children, 31 percent lived in homes where gas was used for cooking, and 69 percent lived in homes where electricity was used for cooking. There was a significant association between parental smoking and the use of gas for cooking. Fathers smoked in 224 (56.4 percent) of the 397 homes where gas was used for cooking, compared to 366 (46.6 percent) of the 786 homes in which electricity was used for cooking ( $\chi^2 = 10.28$ ,  $p < 0.001$ ). Similarly, mothers smoked in 180 (40.8 percent) of the 441 homes in which gas was used for cooking, compared to 292 (33.7 percent) of the 866 homes in which electricity was used for cooking ( $\chi^2 = 6.33$ ,  $p < 0.05$ ). The proportion of children with chronic respiratory symptoms by parental smoking and use of cooking fuel are shown in Table 1.

The use of gas for cooking was associated with an increased risk of hospitalization of the children before age two years because of chest colds and other respiratory illnesses (odds ratio = 2.4) independent of parental smoking (Table 2). Any parental smoking also increased the odds ratio. When both parents smoked in a household in which gas was used for cooking, the odds ratio was 9.25 ( $p = 0.0006$ ). The use of gas for cooking was not associated with increased risk of occurrence of cough with colds in the children. How-

ever, parental smoking increased the risk of occurrence of these symptoms (Table 3). Other than the possibility of wheezing and whistling sounds in the chest with colds, none of the dependent variables in Table 4 was significantly associated with parental smoking and/or use of gas for cooking. Also, the frequency of occurrence of ear infections in the children between ages 0 to two years, or two to five years, or the occurrence of wheezing with exercise was not found to be associated with parental smoking or use of gas for cooking.

The mean standing height of 144.2 cm and weight of 37.8 kg for children whose parents smoked was not significantly different from the mean standing height of 145.6 cm and weight of 38.7 kg for children whose parents did not smoke. Mean values for initial measurements of pulmonary function before the inhaled isoproterenol did not differ significantly between children from smoking and non-smoking families. Significant differences in mean values were not seen after bronchodilator inhalation in the children from non-smoking families, but were apparent among children from smoking families for the measurements of FEF75, FEV<sub>1</sub>, and FEF25-75 (Table 5). The mean values of the measurements of lung volumes for the two groups of children were not statistically different. Because 28 t-tests were performed for these analyses, adjustment was made by accepting only t-tests with p

Table 3—Association of Parental Smoking and Gas Cooking with Occurrence of Cough with Colds in Children

Independent Variables	No. of Children with Symptoms of Coughs with Colds		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	125	252	0.9	0.123	0.55
Electricity	204	495	1.0	...	...
Parental smoking					
Father alone smokes	100	177	1.4	0.224	0.023
Mother alone smokes	36	61	1.5	0.318	0.084
Father and mother smoke	111	173	1.6	0.235	0.082
Either or both parents smoke	247	411	1.5	0.194	0.001
Neither parent smokes	144	366	1.0	...	...

Table 4—Relationship of Parental Smoking and Cooking Gas with Occurrence of Respiratory Symptoms in Children

Independent Variable	No. of Children with Respiratory Symptoms		Odds Ratio	SE	p-Value
	Yes	No			
1. Chest congestion and phlegm with colds					
Gas	70	307	1.1	0.166	0.41
Electricity	126	633	1.0	...	...
Father alone smokes	46	230	1.0	0.213	0.82
Mother alone smokes	19	78	1.3	0.363	0.40
Father and mother smoke	54	229	1.2	0.383	0.28
Either or both parents smoke	119	837	1.2	0.166	0.35
Neither parent smokes	77	403	1.0	...	...
2. Chest congestion and phlegm apart from cold					
Gas	17	345	1.0	0.302	0.99
Electricity	35	708	1.0	...	...
Father alone smokes	12	258	0.9	0.345	0.86
Mother alone smokes	7	87	1.6	0.730	0.30
Father and mother smoke	11	264	0.8	0.317	0.64
Either or both parents smoke	30	609	1.0	0.286	0.98
Neither parent smokes	22	444	1.0	...	...
3. Wheezing and whistling sounds in chests with colds					
Gas	104	273	1.0	0.154	0.56
Electricity	194	564	1.0	...	...
Father alone smokes	74	202	1.2	0.210	0.27
Mother alone smokes	30	67	1.5	0.362	0.12
Father and mother smoke	86	194	1.4	0.241	0.03
Either or both parents smoke	190	467	1.3	0.165	0.03
Neither parent smokes	112	370	1.0	...	...
4. Wheezing and whistling sound in chest apart from colds					
Gas	29	326	0.9	0.222	0.80
Electricity	61	647	0.1	...	...
Father alone smokes	24	235	1.2	0.329	0.52
Mother alone smokes	14	73	2.2	0.761	0.02
Father and mother smoke	16	244	0.6	0.279	0.39
Either or both parents smoke	54	552	1.1	0.257	0.55
Neither parent smokes	36	421	1.0	...	...
5. Attacks of wheezing with shortness of breath					
Gas	30	346	0.7	0.154	0.12
Electricity	83	679	1.0	...	...
Father alone smokes	36	251	0.8	0.211	0.44
Mother alone smokes	12	85	1.1	0.369	0.70
Father and mother smoke	22	261	0.7	0.181	0.14
Either or both parents smoke	60	597	0.8	0.161	0.29
Neither parent smokes	53	429	1.0	...	...

values of  $<0.002$  as significantly different at a 0.05 confidence level ( $0.05 + 28 = 0.002$ ). The mean percentage changes in the pulmonary function measurements (calculated as the differences between the postvalue and prevalue divided by the prevalues for each patient), however, did not differ significantly between the two groups of children (using an unpaired *t*-test).

#### DISCUSSION

Respiratory symptoms and illnesses occur fre-

quently, particularly in the temperate regions of the world in preschool and school-age children. Only recently has it been appreciated that parental smoking at home may be associated with an increased risk of occurrence of respiratory symptoms in children. A higher rate of hospitalization of the children before age two years for chest illnesses (bronchitis, pneumonia, etc) was associated with both parental smoking and gas cooking. A significant increase in pulmonary function after an inhaled bronchodilator among children of

Table 5—Flow Rates of Children Before and After Inhaled Isoproterenol

Variables	Children of Smoking Parents			Children of Nonsmoking Parents		
	Mean (SE) Measurements of Flow Rates and Lung Volumes			Mean (SE) Measurements of Flow Rates and Lung Volumes		
	Preisoproterenol	Postisoproterenol	p*	Preisoproterenol	Postisoproterenol	p*
PEFR	5.11 (0.13)	4.97 (0.13)	0.11	5.10 (0.13)	5.05 (0.12)	0.42
FEF25	4.18 (0.12)	4.15 (0.12)	0.71	4.34 (0.11)	4.23 (0.11)	0.11
FEF50	3.22 (0.09)	3.35 (0.09)	0.02	3.25 (0.09)	3.36 (0.09)	0.07
FEF75	1.52 (0.05)	1.76 (0.07)	0.0001†	1.56 (0.06)	1.69 (0.07)	0.11
FEV <sub>1</sub>	2.23 (0.05)	2.27 (0.05)	0.0002†	2.21 (0.05)	2.23 (0.06)	0.34
FEV <sub>25-75</sub>	2.52 (0.06)	2.52 (0.06)	0.48	2.47 (0.06)	2.50 (0.07)	0.17
FEF25-75	2.60 (0.08)	2.82 (0.08)	0.0001†	2.60 (0.07)	2.78 (0.09)	0.03
FVC	2.55 (0.06)	2.57 (0.06)	0.18	2.51 (0.07)	2.53 (0.07)	0.13

\*Paired t-test comparing initial pulmonary function measurements and postbronchodilator values.

†Significant at 0.05 level after adjusting for the performance of 28 t-tests.

smoking parents is an interesting additional observation perhaps consistent with previous reports of increased bronchial reactivity in cigarette smokers with normal lung function<sup>10</sup> and an association between symptomatic asthma in children and parental smoking.<sup>11</sup>

Parental smoking may be associated with different types of respiratory illnesses in infancy compared to the school age. Fergusson et al<sup>12</sup> found an increased risk of infantile lower respiratory illnesses in the last eight months of the first year of the infant's life to be associated with maternal but not paternal smoking. Similarly, Colley et al<sup>13</sup> found that infantile pneumonia was more common when both parents smoked than when neither parent smoked. The risk was intermediate when only one parent smoked. These results are consistent with our findings that hospitalization of children in the first two years of life for bronchitis and pneumonia was associated with parental smoking. However, Fergusson et al<sup>12</sup> did not study the association of parental smoking and use of gas for cooking on respiratory infection rates. Their study is different from ours also, in that they studied respiratory infection rate between four and 12 months of life. Their study was prospective-retrospective in design, and therefore, parental recall may have been more reliable than in our study. In the first year of life, an infant is likely to spend proportionately more time with the mother than the father. Thus, the age of the child at the time of the administration of the respiratory questionnaire may have been an important factor in the finding that maternal but not paternal smoking was associated with respiratory illness in the child.

Weiss et al<sup>14</sup> reported a dose response between prevalence rate of symptoms of persistent wheezing, cough, and phlegm in children and parental smoking. The rate of occurrence of symptoms in children was highest when both parents smoked, intermediate when either parent smoked, and lowest when no

parent smoked. However, the authors also found a strong association between the occurrence rate of these symptoms in the children and the prevalence rate for such symptoms in the parents. We found a significant association between parental smoking and the prevalence of cough with colds in the children. However, we did not find any association between parental smoking or the use of gas cooking and the reported incidence of cough apart from colds and chest congestion and bringing up phlegm with or apart from colds. In a study of children whose ages were similar to the children in our population, however, Colley<sup>13</sup> found an association between parental smoking and the occurrence of cough during the day or at night in winter in the children. He also found an association between parental smoking and bringing up "any phlegm from the chest first thing in the morning in winter" by the children. The lack of association between these variables and parental smoking in our study may be attributable to the phrasing of the questions in the ATS-DLD questionnaire, where "in the morning" was not specifically mentioned, and where phlegm production was sought in association with chest colds rather than "in winter." Slight changes in the phrasing of questions can result in substantial differences in the type of responses one obtains.<sup>15,16</sup>

Flory et al<sup>17</sup> showed an association between the levels of NO<sub>2</sub> in kitchens and bedrooms of the homes, and the prevalence of respiratory illness in primary school-children. This association was independent of the children's age, sex, social class, and the number of cigarettes smoked at home. In another study, children six to 11 years old from households with gas stoves had a history of more frequent respiratory illnesses before age two years compared to children from homes where gas was not used for cooking.<sup>18</sup> In a study of schoolchildren in England and Scotland, a reported incidence of coughs, colds going to the chest, and bronchitis in children from homes using gas for cooking

was significantly higher than for children from homes where electricity was used.<sup>10</sup> Melia et al.<sup>11</sup> demonstrated that the association between respiratory illness and gas cooking tended to disappear as the children grew older.

The nature of the association of respiratory symptoms in children and gas cooking in the home is yet unclear. Two oxides of nitrogen, nitric oxide (NO) and nitrogen dioxide (NO<sub>2</sub>), are produced in varying concentrations in homes with gas stoves.<sup>12-14</sup> It has been observed that acute exposure of man and animals to high levels of nitrogen dioxide (NO<sub>2</sub>) can cause pulmonary edema and death.<sup>15</sup>

A significant reduction in FEF<sub>25-75</sub> values was observed in children who smoked, as well as in children whose parents smoked but who were non-smokers themselves.<sup>16</sup> At least one group of investigators has found no association between parental smoking and lung function measurements of the children.<sup>17</sup> In these studies, the children did not receive an inhaled bronchodilator drug. Inhaled bronchodilator medication was administered to children in our study, and we observed statistically significant differences in the mean values of FEF<sub>75</sub>, FEV<sub>1</sub>, and FEF<sub>25-75</sub> for children whose parents smoked compared to those whose parents did not smoke. The clinical importance of such observed differences in the absolute values of pulmonary function measurements is, however, unclear.

In a recent study of children six to 11 years old from households with gas stoves, small but significant differences were found in FEV<sub>1</sub> and FVC corrected for height, compared to children from homes where gas was not used for cooking.<sup>18</sup> These families tended to be poorer and were in the lower socioeconomic class. Flory et al.<sup>19</sup> found no significant relationship between lung function measurements and concentrations of NO<sub>2</sub> in either kitchen or bedroom. Lung function measurements of peak expiratory flow rates (PEFR) and FEF<sub>25-75</sub> for children from homes with gas stoves were not significantly higher than measurements for children from homes with electric stoves. Hasselblad et al.<sup>20</sup> however, found pulmonary function suggestively decreased among nine- to 13-year-old girls in homes with gas stoves and not among younger children.

Based on the findings of this report and from previously published findings, one is led to conclude that parental smoking is associated with a risk of certain respiratory illnesses and symptoms among children living in the same environment. An independent but similar effect is suggested for gas cooking. Children from homes where parents smoke had increased reactivity of airways after bronchodilator therapy, but it is not known if these changes persist or have clinical consequences.

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### Myocardial Protection via the Coronary Sinus

The First International Symposium on Myocardial Protection via the Coronary Sinus will be held at the Hotel InterContinental Vienna, Vienna, Austria, February 27-29, 1984. For information, contact the Secretariat, c/o Interconvention, PO Box 80, A-1107 Vienna, Austria.

### Diagnostic Imaging

The Department of Radiology, Duke University Medical Center, will present this five-day postgraduate course at the Hyatt Regency Cancun Hotel, Cancun, Mexico, February 12-17, 1984. For information, contact Donald R. Kirks, M.D., Department of Radiology, Duke University Medical Center, Box 3834, Durham, North Carolina 27710 (919.681-2711, ext 286 or 287).

2023510188



**2023510189**

Lebowitz, M.D., Knudson, R.J., Burrows, B. "Family Aggregation of Pulmonary Function Measurements" Am Rev Respir Dis 120: 8-11, 1984.

SUMMARY: Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data. Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex. Body habitus, as measured by the Ponderal Index, was highly aggregated as well. Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation. After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements. It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

2023510130

# Family Aggregation of Pulmonary Function Measurements<sup>1-3</sup>

MICHAEL D. LEBOWITZ, R. J. KNUDSON, and B. BURROWS

## Introduction

Clinicians have noted that airways obstructive diseases, especially emphysema, appear to run in families, and this has been a common observation since the early nineteenth century (1, 2). Except for the rare homozygotic alpha<sub>1</sub>-antitrypsin deficiency, other genetic predispositions to chronic obstructive diseases have not been clearly demonstrated (3). Studies in England have demonstrated that there is a genetic basis of asthma (4, 5). Recent studies have demonstrated aggregation of pulmonary function in twins (6, 7), and recent population studies have shown that pulmonary function measurements appear to be aggregated in families (8-10).

It has long been recognized that body size and configuration are genetically determined, yielding familial aggregation of body habitus; body habitus has a major influence on pulmonary function. Although adjustment for height to predict a person's lung function is standard, this is not sufficient when examining interindividual correlations of body habitus with lung function. Thus, it is necessary to evaluate the interaction of body habitus in the analysis of familial aggregation of pulmonary function.

This report attempts to examine the relationship of pulmonary function measurements in the family, of body habitus relationships in the family, and the interaction thereof. The influence of a history of airways obstructive disease in parents and children, smoking in parents and children, family size, and the influence of passive smoking, which are possible confounding variables, are examined as well.

## Methods

Data on nuclear families reported herein are derived from the Tucson Epidemiological Studies of Airways Obstructive Diseases, which has been described previously (11). The population under study is a multistage stratified cluster sample of white, non-Mexican-American families in the Tucson area,

**SUMMARY** Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data. Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex. Body habitus, as measured by the Ponderal Index, was highly aggregated as well. Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation. After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements. It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

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where stratification was on age of head of household and on socioeconomic status.

In the first year of this study (1972-1973), questionnaires were completed on all subjects. These included a respiratory history and a family history with a family tree. Subjects 12 yr of age and older completed their own questionnaires. Mothers, or substitutes if the mothers were not available, completed them for children younger than 12 yr of age (11). Comparisons of maternal and self-reporting performed for smoking histories showed no discrepancies. A separate study showed no significant differences, in children 8 to 11, in parental versus self-reporting of chronic symptoms (12). Pulmonary function tests were performed satisfactorily in over 90% of those 6 yr of age and older, using techniques previously described (13).

Nuclear families were defined as families in which there were a mother, a father, and at least one natural child of the pair. There were 344 nuclear families of the 1,635 families studied (approximately 25%). The number of subjects involved in these nuclear families represent about 1,400 of the 3,800 subjects in the total study population. There were 271 families in which both parents and 1 or more of their children had satisfactory pulmonary function measurements in the first year of the study. These were analyzed as units. We also considered relationships between parent-child pairs, spouse pairs, and sibling pairs.

The presence of airway obstructive disease in the children and the parent was obtained from the questionnaires, as was smoking history (for those 15 yr of age and older). Family size, obtained from household records, was also used to determine if it was a confounding variable.

As previously described, all measurements were made by trained nurse inter-

viewers; tests of interobserver variability of all measurements indicated no significant differences (11, 13). Standing height (H) in inches, sitting height in inches, and weight (W) in pounds were used to calculate the Ponderal Index (14), an index of body habitus (i.e.,  $H^3/W$ ). This index had the best correlation with pulmonary function tests when compared with other indexes of body habitus.

The pulmonary function measurements used were: forced vital capacity (FVC) forced expiratory volume in one second (FEV<sub>1</sub>), and maximal expiratory flows at 50 and 75% of the FVC had been expired ( $V_{max_{50}}$  and  $V_{max_{75}}$ , respectively). Each subject's function was first corrected for height and weight, using regression equations derived from data on asymptomatic nonsmokers in this population. These corrected values did not explain all effects of body habitus.

Comparisons of children's and parents' pulmonary function variables (expressed percent predicted) were performed first before accounting for parental body habitus; these were performed before and after Z-score transformations. The Z-scores are standard normal variates; for each subject the observed value was subtracted from:

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group mean and divided by the group standard deviation ( $z_i = (x_{ijk} - \bar{x}_{jk})/s_{jk}$ , for each  $i$  subject,  $j$  age group,  $k$  sex). This removed further effects of age and sex and gave all values the same units. All pulmonary function variables were then adjusted for the individual child's Ponderal Index and the parental Ponderal Indexes (where significantly correlated with the pulmonary function variables) using regression techniques. The Z-scores were recalculated for each of these pulmonary function variables within each age-sex group represented in the parent-child pairs. The Z-score technique is useful for looking at specific effects of other explanatory variables, such as smoking.

Familial aggregation was estimated by analysis of variance (ANOVA), which corresponds to the intraclass correlation as described by Donner and Koval (15). These investigators demonstrated that this method was slightly better than the maximal likelihood estimator if the true correlation was likely to be less than 0.5. Both were better than the usual product-moment correlation method. They also demonstrated that differences in results with inclusion or exclusion of one child were minimal and nonsignificant. The multivariate components of variance method of ANOVA is more useful than other methods of examining aggregation in that it gives separate estimators for variance components and allows usual testing of significance of those estimates. Analyses of variance were performed using the children's pulmonary function measurements as the dependent variable, using age, sex, smoking, and body habitus indexes of the children and the parents as covariates, with parents' pulmonary function (as continuous variables) as the explanatory variables (main effects) in the ANOVA. Covariates were all continuous variables except sex. Main effects were grouped into equal thirds. Two- and three-way interactions were examined. The regression option was used to remove covariate effects, other main effects, and interaction effects from the contribution of each main factor, using SPSS programs on a DEC-10 Cyber 175 University Computer System. In the case of nuclear family analyses using analyses of variance, the analyses were done for all families and separately and for those with 2 or more children (13). For analysis of parent-child pairs, the male/female oldest child was used. For analysis of sibling pairs, the 2 oldest children of each sex in the family were used.

### Results

The characteristics of members of the nuclear families with pulmonary function tests are shown in table 1. There were highly significant product-moment correlations of measures of body habitus between all children and their parents, after adjusting for age and sex.

TABLE 1  
CHARACTERISTICS OF PARENTS AND CHILDREN  
(8 YEARS OF AGE AND OLDER) IN NUCLEAR  
FAMILIES WITH PULMONARY FUNCTION

Characteristics	Children (n = 354)		Mothers (n = 278)		Fathers (n = 289)	
	Mean	SD	Mean	SD	Mean	SD
Age	13.5	5.0	38.1	6.8	38.4	12.2
Height (H) (in.)	60.8	7.5	63.9	2.3	69.3	2.5
Weight (W) (lb.)	108.4	41.8	134.9	34.8	172.9	34.8
H/W <sup>1/3</sup>	13.1	0.8	12.3	0.7	12.5	0.5
%FVC	110.3	23.9	102.3	18.5	101.2	18.0
%FEV <sub>1</sub>	108.5	21.3	104.8	18.9	104.2	17.8
Ever smokers, %	1.7*		80.0		72.3	

Definition of abbreviations: %FVC = percent predicted forced vital capacity; %FEV<sub>1</sub>, a percent predicted forced expiratory volume in one second.

\* n = 181, 18 yr of age and older only.

The linear regression of all the children's H/W<sup>1/3</sup> on mothers' H/W<sup>1/3</sup> had a correlation ( $r$ ) of 0.804 ( $p < 0.0001$ ); with fathers,  $r$  was 0.773 ( $p < 0.0001$ ). There were also some significant product-moment correlations of the amount of smoking (pack-years) between various pairs, especially between fathers and children siblings and spouses ( $p < 0.001$ ), even though many fewer children than parents smoke. The significant correlations were between father and both daughters and sons, between siblings, and between spouses; the mothers-sons correlation of smoking was borderline ( $p = 0.085$ ). There was no correlation of smoking with any of the measurements of body size or habitus.

Product-moment correlations between children's and parents' pulmonary function measurements were statistically significant ( $r$  as much as 0.30) prior to adjusting for covariates. The most significant aggregation of a pulmonary function measurement prior to body habitus correction was with FVC, which as a volume measurement is most closely correlated with body habitus. The relationships were also strong and significant for FEV<sub>1</sub>, but were less often significant for the flow variables.

However, regressions of the children's percent predicted pulmonary function against parents' pulmonary function and body habitus measurements showed significant correlations of the children's pulmonary function with the parents' body habitus, as well as with their own body habitus. After body habitus and age corrections, the previous correlations of pulmonary function variables between any of the pairs were no longer present. Thus, the relation between children's lung function and parents' lung function is likely to be related to their similar body habitus.

Despite the aggregation of asthma (table 2), it was not a factor in the aggregation of pulmonary function measurements when tested by ANOVA. There was no family aggregation of present diagnosed chronic bronchitis for emphysema. The presence of these other airway obstructive diseases in parents and/or children were not factors in the relationships between pulmonary function measurements in the family (by ANOVA). Family size was not found to be a significant factor in any of the analyses. Analyses of variance for families with 2 or more children only, as well as for all families (1 child or more), yielded similar results.

TABLE 2  
PHYSICIAN-CONFIRMED EVER ASTHMA IN NUCLEAR FAMILIES

	No Asthma in Parents	One Parent with Asthma	Both Parents With Asthma
Families, n	273	88	3
Families with 1+ asthmatic child, %	10.8*	28.5	100
Oldest children with asthma, %	5.3	19.1	33.3
Children, n	838	122	11
Children with asthma, %	5.5*	19.7	83.8

\* Rates of asthma significantly higher with one or more asthmatic parents ( $p < 0.001$ ).

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TABLE 3  
CHILDREN'S VOLUME AND FLOW MEASUREMENTS IN RELATION TO PARENTS' VOLUME AND FLOW MEASUREMENTS, CONTROLLING FOR OTHER VARIABLES (BY ANOVA)\*

	df	FVC			$\dot{V}_{max_{25}}$		
		Mean Square	F	p	Mean Square	F	p
<b>No controls</b>							
Father's function	2	3,086.1	6.97	0.001	1,837.5	2.57	0.078
Mother's function	2	2,348.4	4.84	0.008	1,551.8	2.44	0.088
Interaction	4	319.9	0.99	0.800	417.1	0.86	0.824
Explained	8	1,758.2	3.78	0.001	877.4	1.84	0.148
<b>Age, sex, and smoking controls</b>							
Covariate <sup>†</sup>	5	4,195.3	16.88	0.001	2,742.5	4.88	0.001
Father's function	2	918.8	2.38	0.084	1,031.3	1.76	0.174
Mother's function	2	1,389.2	3.55	0.030	1,478.8	2.52	0.083
Father's smoking	2	286.8	0.70	0.499	1,266.5	2.33	0.089
Mother's smoking	2	42.6	0.11	0.895	1,128.6	1.93	0.148
2-way interactions <sup>‡</sup>	24	482.3	1.25	0.199	883.1	0.99	0.918
Explained	37	1,378.2	3.31	0.001	1,052.1	1.80	0.808
<b>Age, sex, and habitus controls,<sup>‡</sup> adjusted children's function<sup>†</sup></b>							
Covariate <sup>†</sup>	4	1,462.8	8.72	0.001	1,531.8	2.85	0.040
Father's function	2	811.4	2.00	0.138	408.1	0.84	0.529
Mother's function	2	274.9	1.08	0.343	88.1	0.14	0.874
2-way interactions	24	487.9	1.91	0.008	944.9	1.48	0.078
3-way interactions	32	382.1	1.49	0.052	420.4	0.86	0.821
Explained	88	823.4	2.44	0.001	770.5	1.21	0.163

Definition of abbreviations: df = degrees of freedom; FVC = forced vital capacity;  $\dot{V}_{max_{25}}$  = maximal flow after exhalation of 25% of FVC; F = variance ratio.

\* "Regression option" (see text).

† Total = 257 without habitus controls, less with habitus data, as complete data missing from 1 or more members of some families.

‡ Parents' habitus also as main effects.

§ No three-way interactions.

|| Children's function adjusted for their and parents' body habitus using the Ponderal Index.

¶ All ages, children's sex and smoking/habitus.

To account for all of the possible significant covariates and interactions, we used multivariate analysis of variance to evaluate aggregation of FVC, FEV<sub>1</sub>,  $\dot{V}_{max_{25}}$ ,  $\dot{V}_{max_{50}}$ . Each explanatory variable was treated as an independent contributor to the dependent variable. The results for all 4 pulmonary function variables were similar, so only 1 volume (FVC) and 1 flow ( $\dot{V}_{max_{25}}$ ) variable are shown (table 3).

Without covariate controls or adjusted children's pulmonary function, the parents' volume measurements contributed significantly to the explanation of the children's measurements. These significant relationships for FVC, FEV<sub>1</sub>, and  $\dot{V}_{max_{25}}$  were also present after age and sex were used as covariates and parental smoking was used as explanatory variables (table 3). However, adjusting for smoking reduced the significance of fathers' FVC and both parents'  $\dot{V}_{max_{25}}$ . Parents' smoking was significant only for  $\dot{V}_{max_{25}}$  (maternal smoking only). Furthermore, we did not find any relation between fathers' or mothers' smoking and their spouses' pulmonary function.

The body habitus-corrected FVC and

$\dot{V}_{max_{25}}$  of the children as the dependent variables had no significant relationship with any of the explanatory variables, where both the parents' pulmonary function variables had been corrected for body habitus as well. The total amount of variability explained in these analyses was significant for FVC and FEV<sub>1</sub> ( $p = 0.001$ ).

The analyses of variance performed on the pulmonary function measurements of parent-oldest child, spouse, or sibling pairs yielded negative results.

There were two exceptions to this: the contribution of the father's  $\dot{V}_{max_{25}}$  on the daughter's  $\dot{V}_{max_{25}}$  was significant ( $p = 0.046$ ); however, the total variance explained was not significant. As that only left 1 of 24 comparisons significant, mother-son FVC ( $p$  of main effect = 0.028), and one might expect approximately 1 of these many comparisons ( $n = 24$ ) to be significant by chance alone (at  $p < 0.05$ ), this was considered a chance finding. Performing the same analyses after correcting for smoking habits in the parents and children, and after analyzing by whether airways obstructive diseases were present or not, did not change the results.

The children's Z-score-corrected pulmonary function variables were compared among smoking and nonsmoking parents; the results are shown in table 4. As can be seen, parental smoking did not have a significant effect on children's pulmonary function; smoking habits of others in the household (predominantly siblings) did not have any effect either.

## Discussion

It is generally agreed that body habitus is genetically determined; it certainly has high familial aggregation. Pulmonary function variables are measurements that are highly dependent on various characteristics of body habitus. Pulmonary function measurements have previously been shown to aggregate in families when body habitus in the families was not accounted for (8, 9). In our study, we first saw strong correlations between parents' and children's pulmonary function measurements, significant for FVC, FEV<sub>1</sub>, and  $\dot{V}_{max_{25}}$ . However, when we controlled for body habitus in the examination of the relationship between parents' and

TABLE 4  
Z VALUES OF CHILDREN'S PULMONARY FUNCTION BY PARENTAL SMOKING

Parental Smoking	n	FVC		FEV <sub>1</sub>		$\dot{V}_{max_{25}}$		$\dot{V}_{max_{50}}$	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Neither	48	-0.08	1.00	-0.12	0.99	-0.16	1.19	-0.08	1.08
Mother smokes	35	-0.16	0.83	-0.16	0.81	-0.15	0.95	0.0	0.88
Father smokes	92	-0.06	0.91	-0.04	0.97	-0.17	0.95	-0.17	1.01
Both smoke	86	+0.19	1.08	+0.23	1.08	+0.15	0.99	+0.20	0.97
Total	271	0.01	0.89	0.03	1.00	0.0	1.00	0.0	1.00
		df	Mean Square	df	Mean Square	df	Mean Square	df	Mean Square
Between		3	1.578		2.212		1.388		2.314
Within		267	0.987		0.975		0.982		0.982
F			1.622		2.288		1.398		2.358
p			0.182		0.081		0.244		0.072

For definition of abbreviations, see table 3.

children's pulmonary function measurements, we no longer found such relationships. Thus, familial correlations for observed pulmonary function, especially FVC, were dependent on familial aggregation of body habitus, even after controlling for age and sex. It can not be construed as an overadjustment of familial data, as the underlying familial aggregation is one of body habitus characteristics. This is more a genetic effect than one of dietary or environmental effect, as shown by the weaker relationship between siblings and the lack of a relationship of body habitus between spouses.

On the other hand, we did detect a familial relationship of asthma between children and parents independent of smoking and pulmonary function measures (table 2), which confirmed findings of Sibbald and coworkers (4, 5), and Townley and associates (16). To insure that this is not strictly a result of reporting bias, objective measures such as bronchial-reactivity would have to be done to confirm the relationship, as has been done by Townley and associates (16). This familial aggregation of asthma did not affect the findings for any familial aggregation of pulmonary function.

We found also that smoking habitus aggregated in families but was probably an environmental influence only. Spouses and siblings had the closest relationships of smoking habits ( $r = 0.29$  and  $0.50$ , respectively). Smoking habits of both sons and daughters correlated more highly with those of their fathers ( $r = 0.22$  and  $0.23$ , respectively) than with those of their mothers ( $r = 0.08$  and  $0.03$ , respectively).

Previously, we had not found a relationship between children's and parents' chronic symptoms by parental smoking (20). When we examined effects of parental smoking on children's pulmonary function, taking into account the initial relationship between parental and children's pulmonary function, only maternal smoking was a significant explanatory variable, and

only for  $\dot{V}_{max}$  ( $p = 0.043$ ). Considering the number of ways in which the comparisons were made, this one difference probably was not meaningful. When children's pulmonary function was adjusted for paternal body habitus as well as their own, there was no significant parental smoking contribution. A lack of a relationship between parental smoking and children's pulmonary function, even without correcting for parental pulmonary function or body habitus, had been reported by Speizer and coworkers (17, 18), Schilling and associates (10), and Dodge (12). Tager and colleagues (19) had reported this association, but it too might disappear if corrected for the family aggregation they found (9), and/or body habitus. It is possible that controlling for body habitus in a family may be controlling for other genetic and host factors as well.

Finally, we did not find any significant interaction between the smoking habits of either parent smoking and their spouses' lung function (table 3), similar to Comstock and coworkers (21) and Schilling and associates (10), but different from Kauffmann and coworkers (22).

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2023510194



Berwick, M., Zagraniski, R.T., Leaderer, B.P., Stolwijk, J.A.J.  
"Respiratory Illness in Children Exposed to Unvented Combustion  
Sources" Indoor Air: Radon, Passive Smoking, Particulates and  
Housing Epidemiology Volume 2: 255-260, 1984.

ABSTRACT. Using a staged design of air quality monitoring, we followed 174 families using unvented kerosene heaters and 173 families without heaters for a three-month period to evaluate the association between nitrogen dioxide (NO<sub>2</sub>) exposure and acute respiratory illness rates. Environmental and health data were obtained through personal interview, bi-weekly telephone interviews, tax assessor records, and from two-week integrated NO<sub>2</sub> measurements in 303 residences. One hundred-twenty-one children under age 13 were followed in this study, 59 living in homes with kerosene heaters and 62 living in homes without. Initial analyses indicate that exposed children have significantly more days of acute respiratory illness than controls. Limitations are imposed by sample size and by possible selection bias.

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# INDOOR AIR

Volume

**2**

## **Radon, Passive Smoking, Particulates and Housing Epidemiology**

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# **Proceedings of the 3rd International Conference on Indoor Air Quality and Climate**

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2023510201

# CONTENTS

	Page
<b>RADON IN DWELLINGS: EXPOSURE AND RISK ANALYSIS</b>	<b>13</b>
Nazaroff, W W Nero, A V	Transport of radon from soil into residences 15
Jonassen, N McLaughlin, J P	Airborne radon daughters, behavior and removal 21
Edling, C Wingren, G Axelson, O	Radon daughter exposure in dwellings and lung cancer 29
<b>RADON: EXPOSURES AND RISKS</b>	<b>35</b>
Swedjemark, G A Hjones, L	Exposure to the Swedish population to radon daughters 37
Fenyves, E J Kinslow, R H	Indoor radon concentrations in public buildings 45
Put, L W de Meijer, R J	Survey of radon concentrations in Dutch dwellings 49
Papastefanou, C Manolopoulou, M Savvides, El Charalambous, St	Exposure from radon and radon daughters in dwellings 55
Brown, L Green, B M R Miles, J C H Wrixon, A D	Radon exposure of the UK population 61
Burkart, W Wernli, C Brunner, H	Assessment of additional exposures and risks from airtightening of homes in an Alpine area with high radon emanation 67
Pershagen, G Damber, L Falk, R	Exposure to radon in dwellings and lung cancer: A pilot study 73
Bergman, H Edling, C Axelson, O	Indoor radon daughter concentrations and passive smoking 79
Wilson, C	Mapping the radon risk of our environment 85
Radford, E P St Clair Renard, K G	Application of studies of miners to radon problem in homes 93

2023510202

# RADON: SOURCES AND MEASUREMENT

Downard, T R Geiger, E L Millard, J B	Field evaluation of Eberline's radon daughter working level monitor	99
Oswald, R A Alter, H W	Localization of indoor radon sources using integrating track etch detectors	105
Paripas, B Takacs, S Somogyi, Gy Nikl, I	Integral alpha and gamma radiation measurements in dwelling houses	113
Schmied, H	The sensitivity to humidity of radon monitoring instruments	119
Gustafsson, J Nilsson, I	Tracing of radon leakages	125
Hawthorne, A R Gammage, R B Dudney, C S	Effect of local geology in indoor radon levels: A case study	137
Kochari, B K	Contribution of soil gas, potable water, and building material to radon in US homes	143
Keller, G Folkerts, K H	A study on indoor radon	149
Jönsson, G	Radon measurements in Sweden. Some results	155
Martell, E A	Aerosol properties of indoor radon decay products	161

# FIBRES AND PARTICULATES IN THE INDOOR ENVIRONMENT

van Houdt, J J Boisij, J S M	Mutagenic activity of indoor airborne particles compared to outdoors	169
Seifert, B Dreus, M Aurand, K	Indor heavy metal exposure of the population around a secondary lead smelter	177
Schneider, T	Man-made mineral fibers (MMMF) and other fibers in the air and in settled dust	183
Sega, K Kalinic, M Sisovic, A	Indoor-outdoor relationships for respirable particles, total suspended particle matter and smoke concentrations in modern office buildings	189
McCarthy, S M Colome, S D Spengler, J D	Indoor and outdoor aerosols: A multivariate approach to source identification	195

2023510203

		9
FIBRES AND PARTICULATES: CHARACTERIZATION AND RISKS		201
Wechsler, C J Fong, K L	Characterization of organic species associated with indoor aerosol particles	203
Meckler, M	Analysis of low particulate size concentration levels in office environments	209
Janka, K Kuimala, V	Optical particle counter as a wide range, continuous monitor for particle concentrations	215
Rindal, A	Man-made-mineral fibres (MMMF) in indoor climate	221
Gunnarsson, M Bergström, B	Are man-made mineral fibres responsible for the development of bronchitis and atelectasis of the lung?	225
Tockman, M S Wheeler, P Frost, J K Bell Jr, W Levin, M Green, K	Pleural changes consistent with asbestos exposure found on screening radiographs are not predictive of lung cancer	229
EPIDEMIOLOGICAL STUDIES OF HEALTH DISORDERS RELATED TO HOUSING		235
Iversen, M Bach, E Lundqvist, G R	A prospective study of the health and comfort changes among tenants after retrofitting of their flats	237
Matsuki, H Yanagisawa, Y Osaka, F Kasuga, M Nishimura, R	Personal exposure to NO <sub>2</sub> and its health effect with urinary hydroxyproline to creatinine ratio as biochemical indicator	243
Valbjörn, O Kousgård, M	Headache and mucus membrane irritation. An epidemiological study	249
Berwick, M Zagraniski, R T Leaderer, B P Stolwijk, J A J	Respiratory illness in children exposed to unvented combustion sources	255
Lets, R Quackenbush, J J Spengler, J D	Effects of choice of exposure index in NO <sub>2</sub> epidemiological studies	261

2023510204



		10
HOUSING EPIDEMIOLOGY		267
Goldstein, I Hartel, D Andrews, L	Indoor exposure of asthmatics to nitrogen dioxide	269
Loewenstein, J C Bourdel, M C Maffiolo, G Krainik, F Wolmark, Y	Relation of environmental conditions to the health of the elderly in a long term care hospital: A longitudinal survey	275
Mage, D T	A possible relationship of sudden infant death syndrome to indoor air quality	281
Speizer, F E Ware, J Dockery, D Ferris Jr, B G	Lack of effect of gas stoves on longitudinal change in lung function in children ages 6-11 years	287
PASSIVE SMOKING AND HEALTH EFFECTS		295
Weber, A	Environmental tobacco smoke exposure: acute effects - acceptance levels - protective measures	297
Schmidt, F	Passive smoking as a real risk to health	303
Ferris Jr, B G Dockery, D W Ware, J H Berkey, C S Speizer, F E	Effects of passive smoking on children in the six-cities study	309
Hoffmann, D Brunnemann, K D Adams, J D Haley, M J	Indoor air pollution by tobacco smoke: Model studies on the uptake by nonsmokers	313
Hugod, C	Passive smoking - a source of indoor air pollution	319
PASSIVE SMOKING: CHARACTERIZATION AND COUNTERMEASURES		327
Sterling, T D	Effects of restricting and prohibiting smoking in office environments on reactions of office personnel to environmental health and stress factors	329
Matsushita, H Mori, T	Nitrogen dioxide and nitrosamine levels in indoor air and side-stream smoke of cigarette	335

2023510205

		11
Lehti, H	Ashtray	341
Vertio, H		
Ramstedt, L M	Smokers' and non-smokers' perception of passive smoking and certain control measures	345
Winnke, G	Patterns and determinants of reaction to tobacco smoke in an experimental exposure setting	351
Plischke, K		
Roscovanu, A		
Schlipkoetter, H W		

2023510206

RESPIRATORY ILLNESS IN CHILDREN EXPOSED TO  
UNVENTED COMBUSTION SOURCES

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Abstract

Using a staged design of air quality monitoring, we followed 174 families using unvented kerosene heaters and 173 families without heaters for a three-month period to evaluate the association between nitrogen dioxide ( $\text{NO}_2$ ) exposure and acute respiratory illness rates. Environmental and health data were obtained through personal interview, bi-weekly telephone interviews, tax assessor records, and from two-week integrated  $\text{NO}_2$  measurements in 303 residences. One hundred-twenty-one children under age 13 were followed in this study, 59 living in homes with kerosene heaters and 62 living in homes without. Initial analyses indicate that exposed children have significantly more days of acute respiratory illness than controls. Limitations are imposed by sample size and by possible selection bias.

Introduction

Unvented combustion in homes can lead to high ambient levels of several air contaminants with nitrogen dioxide ( $\text{NO}_2$ ) being the most notable (1). While  $\text{NO}_2$  has been implicated as a potentiator of lower respiratory infections in laboratory animals (2), the epidemiologic evidence for determining unhealthy levels in humans is inconclusive at this time. Melia *et al.* (3,4) and Florey *et al.* (5) have reported data that suggest that children between the ages of 5 and 11 living in homes with gas cooking stoves had higher levels of acute respiratory symptoms or disease than those living in homes with electric cooking stoves. The range of  $\text{NO}_2$  exposures measured in these studies was from 8-634  $\mu\text{g}/\text{m}^3$ . The generalizability of these studies is limited by low

2023510207

response rates and an overrepresentation of lower socioeconomic status groups.

Keller *et al.* (6,7) found no difference in illness rates between volunteers who lived in homes using gas for cooking and those using electricity. The range of  $\text{NO}_2$  exposures in their study was reported for a sample of homes only and was very low ( $22 \text{ ug/m}^3$ ), so that it was unlikely that any positive association could be found. The potential for recall bias limits the finding of Speizer *et al.* (8) that children living in homes with gas cooking stoves had higher respiratory illness rates before age two than children living in homes using electricity stoves. Dodge (9) reported that exposure to parental smoking and gas cooking was associated with higher respiratory symptom rates in Arizona schoolchildren. However, his sample is unrepresentative, suffered from low response rates, and no pollutant measures were made.

The investigation reported here was designed to determine whether exposure to air contaminants emitted by kerosene space heaters, particularly  $\text{NO}_2$ , is associated with excess respiratory illness in children. We hypothesized that there was a positive correlation between  $\text{NO}_2$  levels and acute respiratory illness rates among children. We identified a population with kerosene heaters where we could measure the household  $\text{NO}_2$  exposures of children while accounting for many of the other potential risk factors for respiratory infections, such as parental smoking, presence of gas appliances, household size, school attendance, socioeconomic status, age, and previous history of respiratory infections.

#### Methods

Study Design and Population. To allow the most precise yet efficient estimation of individual exposures to pollutants, a staged design of air quality monitoring was employed in a cohort study. A cohort of adults who bought kerosene heaters was identified from lists obtained from local kerosene heater dealers in Connecticut. A control household was systematically chosen from the neighborhood of an exposed household. Neighborhood controls were selected to control ambient air quality and socioeconomic status. In each household an index woman, the oldest woman residing in the house, and an index child (if a child lived in the house), the child nearest in age to 5 but less than 13, were chosen to participate in the study. Households with no adult female present and households no longer using kerosene heaters were excluded from the study.

If subjects agreed to participate, an initial questionnaire was administered. Information was obtained about building characteristics, user heating patterns, and the health history and current respiratory symptomatology of the index adult and the index

2023510208

child (if present). Subjects were then followed up by telephone bi-weekly for 12 weeks during January-March 1983 to obtain respiratory symptoms for the female and the child (if present) and heater use patterns during the previous two weeks period. As described in a separate paper (10) air monitoring for NO<sub>x</sub> was conducted for at least one two-week period in 87.3 percent of the study households. The study population analyzed here consists of 121 children under age 13. Fifty-nine lived in homes with kerosene heaters; 62 lived in homes without. All children were Caucasian.

Definition of Variables. The independent variables used in these analyses included: (1) demographic factors: age, sex, socioeconomic status [SES, Hollingshead Index(11)]; (2) exposure parameters: number of minutes of gas cooking per day (total estimated oven and burner use), number of cigarettes normally smoked daily at home by all residents, school enrollment, type of cooking fuel, total household size (a proxy for density), average daily hours of kerosene heater use for each two-week period, one two-week average measurement of NO<sub>x</sub> in each residence, and (3) respiratory illness history. "Respiratory illness history" was a continuous variable derived by adding each serious respiratory disease reported in the initial questionnaire (i.e. ever had pneumonia) and the average number of chest colds per year (estimated by the mother).

We used the reported average hours of kerosene heater use during each two-week period as a proxy for NO<sub>x</sub> exposure. Average hours of heater use (by household) correlates fairly well with integrated average NO<sub>x</sub> measurements ( $r = 0.70$ ,  $p < 0.001$ ). The variable, average hours of heater use, was available for each child for each of 6 periods.

The dependent variable used in multivariate analysis, days of illness, was not normally distributed, so we dichotomized it as one or more days of illness and no days of illness and used linear logistic regression following the methods of Harrell (12). SAS 82.3 programs were used for nonparametric analyses and the linear logistic regression. For variables that were normally distributed (i.e. age, household size, etc.), we computed means, t-tests, and correlations using StatPac (13) on the IBMPC.

### Results

Participation and Demographic Factors. The household participation rate among the exposed group was 77.9 percent and 80.7 percent among the unexposed. The loss to follow-up over the study period was 3.4 percent among the exposed group and 5.7 percent among the unexposed.

There were no statistically significant demographic differences

between the exposed and unexposed groups of children. The mean age of the children studied was 6.8 years, the mean household size was 4.2 persons per household, the mean index of SES was 43.4, and the mean index of history of respiratory illness was 2.7.

Exposure Factors. There was more gas cooking in the unexposed children's homes (46.5 minutes/day) when compared to the exposed children's (17.5 minutes/day),  $t$ -test=1.82,  $p = 0.07$ , two-tailed; however, since so few children's homes had gas stoves (8 exposed, 13 unexposed), there were not enough data for meaningful use in the present analysis. There was no statistically significant difference in the mean number of cigarettes smoked daily in children's homes (12.63 exposed, 12.74 unexposed). Average two-week integrated  $\text{NO}_2$  samples were taken in 113 of the 121 children's homes in four places: outdoors, in the kitchen, in a living room, and in an adult's bedroom. The mean outdoor level of  $\text{NO}_2$  for exposed households was 14.62  $\mu\text{g}/\text{m}^3$  (range 5-43  $\mu\text{g}/\text{m}^3$ ) and 12.70  $\mu\text{g}/\text{m}^3$  (range 0-26  $\mu\text{g}/\text{m}^3$ ) for unexposed households. The mean kitchen level of  $\text{NO}_2$  in homes with kerosene heaters was 46.92  $\mu\text{g}/\text{m}^3$  (range 3-211  $\mu\text{g}/\text{m}^3$ ) and 14.07  $\mu\text{g}/\text{m}^3$  (range 0-80  $\mu\text{g}/\text{m}^3$ ) in homes without kerosene heaters. The mean living room level of  $\text{NO}_2$  in children's homes with kerosene heaters was 46.84  $\mu\text{g}/\text{m}^3$  (range 3-134  $\mu\text{g}/\text{m}^3$ ) and 10.36  $\mu\text{g}/\text{m}^3$  (range 0-63  $\mu\text{g}/\text{m}^3$ ) in children's homes without kerosene heaters. The mean level of  $\text{NO}_2$  found in bedrooms in exposed homes was 46.82  $\mu\text{g}/\text{m}^3$  (range 3-225  $\mu\text{g}/\text{m}^3$ ) and 10.4  $\mu\text{g}/\text{m}^3$  (range 0-66  $\mu\text{g}/\text{m}^3$ ) in bedrooms in unexposed homes. The overall average use of kerosene heaters was 7.7 hours per day (range 0-24 hours per day).  $\text{NO}_2$  measurements in children's homes with kerosene heaters were on average 3-4 times as high as in homes without heaters.

Association between exposure and acute respiratory illness. First, in order to determine whether kerosene heater exposure had an association with the days of illness, nonparametric statistical tests were applied to the data. Children exposed to kerosene heaters and children not exposed to heaters were ranked as to the total number of days sick over the 12 week follow-up period. A Wilcoxon rank sum test was performed using the  $t$ -approximation for the significance levels. Children living in homes with kerosene heaters had significantly more days of illness than children living in homes without kerosene heaters ( $t=2.14$ ,  $p < 0.05$ ).

Next, rank correlations were carried out between all independent variables and the dependent variable, days of illness. There was little association between average hours of heater use and number of days sick over the entire period (Spearman correlation coefficient,  $r_s = 0.06$ ,  $p = 0.09$ ). Age and history of respiratory illness were more strongly associated with days of illness ( $r_s = 0.344$ ,  $p < 0.01$ ,  $r_s = -0.17$ ,  $p < 0.05$ , respectively).

Finally, linear logistic regression was used to determine which variables were significantly associated with one or more days of

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illness during each two-week period while adjusting for other measured potential risk factors. Average hours of heater use per day were significantly associated with days of illness ( $p < 0.05$ ) while controlling for type of cooking fuel, cigarettes smoked per day, household size, sex, age, school enrollment, and history of respiratory illness. Age had a significant, inverse association with days of illness ( $p < 0.05$ ). History of respiratory illness was positively associated ( $p < 0.05$ ). SES was marginally associated ( $p = 0.07$ ).

#### Discussion

This initial analysis suggests that young children with a history of respiratory infections are the most sensitive to the adverse health effects of  $\text{NO}_2$  (or kerosene heater exposure). These results are consistent with previous studies that have shown that exposure to gas cooking has no effect on respiratory illness in women and school-age children (6,7), a borderline association with 5-11 year-olds (2,3,4) and an association with the history of respiratory illness in children under 2 years(7). The effects seem to be the most pronounced in young age groups. It should be emphasized that the results presented are preliminary.

These data are subject to many potential biases, some of which are: [1] recall bias in terms of reporting appliance use; [2] a limited ability to generalize from a convenience sample; [3] the publicity surrounding the safety of kerosene heaters; [4] all heater-owners had operated their heaters for at least one season prior to the study; as many as 34 potentially sensitive people were not eligible because they no longer used their heaters due to odor or hypersensitivity. A final limitation is the small sample size.

Further research should concentrate on studying the association between  $\text{NO}_2$  exposure and younger-aged children.

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Gardner, G., Frank, A.L., Taber, L.H. "Effects of social and family factors on viral respiratory infection and illness in the first year of life" Journal of Epidemiology and Community Health 38: 42-48, 1984.

ABSTRACT. A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness and evaluated for the relationship that these had to certain social and familial factors. The results showed no general patterns of association between viral infection and the study factors, but there were several significant individual associations. Excess influenza virus infection was found for black infants, infants with at least one sibling, and especially those with school age siblings. Rhinovirus infection rates were highest among girls attending daycare. In addition, significantly higher rates of lower respiratory disease (LRD) were seen in daycare infants and low socioeconomic infants and a definite trend to increasing amounts of LRD was seen with increasing family size. Protection from LRD seen in girls was apparently lost in daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor.

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MARCH (1)

## Effects of social and family factors on viral respiratory infection and illness in the first year of life

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**SUMMARY** A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness and evaluated for the relationship that these had to certain social and familial factors. The results showed no general patterns of association between viral infection and the study factors, but there were several significant individual associations. Excess influenza virus infection was found for black infants, infants with at least one sibling, and especially those with school age siblings. Rhinovirus infection rates were highest among girls attending daycare. In addition, significantly higher rates of lower respiratory disease (LRD) were seen in daycare infants and low socioeconomic infants and a definite trend to increasing amounts of LRD was seen with increasing family size. Protection from LRD seen in girls was apparently lost in daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor.

Viral respiratory illness is a major cause of morbidity and mortality in infancy. Children under 1 year of age have the highest incidence of acute respiratory illness<sup>1-4</sup> and most are apparently caused by viruses.<sup>1</sup>

Social and family factors influence the incidence of illness during infancy<sup>5-7</sup> but documented infection rates have been less frequently studied. For this reason we examined both infection and illness during the first year of life of 131 infants followed up in the Houston Family Study between 1975 and 1980.

### Materials and methods

#### RECRUITMENT AND MONITORING

General methods used in the Houston Family Study have been reported previously.<sup>1,8</sup> A total of 131 infants were observed for the first year of life from 1975 to 1980. In 1975-6 recruitment of pregnant women took place at Jefferson Davis, a county hospital; thereafter all recruiting was from the community at large at an average of two or three families a month. The infants had blood obtained at birth (cord blood) and at 4, 8, and 12 months of age. Home visits were made every week during the respiratory virus season (biweekly at other times) for history and physical examination and to obtain nasal wash specimens for virus culture from infants. Additional home or clinic visits were made as needed

for sampling of all illnesses. Diagnoses were made by a physician, nurse, or physician's assistant.

Records of all clinical contacts were available for review of illnesses. Upper respiratory illnesses (URI) were categorised as afebrile, febrile, or otitis media. For lower respiratory disease (LRD), the categories were laryngotracheobronchitis (LTB), bronchiolitis, or pneumonia. On review, illnesses lasting more than two weeks could usually be reinterpreted as two or more illnesses. When difficulty arose as to the nature or duration of an illness, the impressions of people seeing the child during the illness were used.

#### LABORATORY METHODS

Tissue cultures used for virus isolation were rhesus monkey kidney, MDCK, LLC-MK2, HEP-2, and WI-38.<sup>10-12</sup> Some specimens were inoculated into fertilised hen's eggs.<sup>13</sup> Serological tests included haemagglutination inhibition for influenza A and B<sup>14</sup> and microneutralisation for respiratory syncytial virus (RSV), parainfluenza virus types 3 (para 3),<sup>15</sup> and influenza A and B.<sup>16</sup> Fourfold rise in antibody titre (or failure of passively acquired antibody to fall) was considered evidence of infection.

#### SOCIAL AND FAMILY FACTORS

Personal and family data were obtained on enrolment and then recorded for each subsequent

year. Six factors were studied: sex, race, parental smoking, socioeconomic class, number of siblings, and attendance at daycare. Race was white or non-white with the latter including blacks and Mexican-Americans. An infant was considered exposed to parental smoking if either mother or father or a live-in relative smoked five or more cigarettes a day. An infant was considered a daycare attender if attendance at a daycare facility or mother's day out (sponsored by local churches) was consistent for at least five months. Finally, socioeconomic class was "low" if the family was eligible for the county hospital or made less than \$12 000 a year, "medium" if the family had private medical insurance or made more than \$12 000 a year, and "high" if the family had private medical insurance, made more than \$12 000 a year, and one or both parents had attended at least three years of college.

#### ANALYSIS

Viral infection and respiratory illness rates were analysed for each family factor category. The mean number of infections or illnesses was calculated from the total number of episodes and reported as the rate per 100 child years. Chi-square analysis was done on the distribution of the data.

#### Results

From 1976 to 1980, 92 infants (including three sets of twins) from 75 families were followed up. There were 59 whites, 24 blacks, and nine Mexican-Americans. Forty two per cent of the black and Mexican-American families were in the low socioeconomic group compared with 15% of the white families. The 39 infants studied from spring 1975 to spring 1976 will be included in selected analyses only because of socioeconomic imbalance (38 of 39 in low socioeconomic class) and some limitation in detailed clinical information on minor or non-influenza A illnesses, or both, during this first study year. This group was composed of 13 white, 21 black, and five Mexican-American infants.

#### VIRUS INFECTION

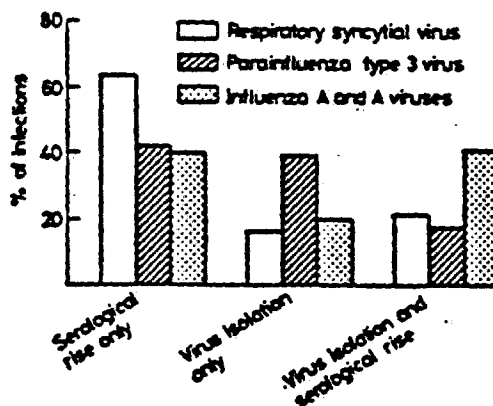
The figure shows the number of infections documented for the four viruses where serology was used in addition to virus isolation. Respiratory syncytial virus (RSV) had the largest proportion of infections identified by serological methods alone (63%). Of 40 influenza A and B infections (35 type A and five type B), 40% were identified by serology alone. In addition, 42% of the parainfluenza type 3 (para 3) infections were identified by serology alone. The remainder of the infections shown in tables 1 and 2 for these four agents were identified by isolation alone or isolation plus fourfold serological rise.

Table 1 shows the virus infection according to the selected social and family factors. In general, these factors were not significantly related to rates of proved viral infection. There were, however, some interesting exceptions.

Adenovirus infection rates were significantly associated with the number of siblings and daycare attendance. Infants with one sibling had the highest rate of infection while those with no siblings had the lowest. Infants with one sibling more often attended daycare (41%) when compared with those with none or two or more sibling infants (19% and 15% respectively); this may have influenced the chi square results. Numbers became too small when further analyses of daycare by number of siblings was done for adenovirus infection so the influence of the two factors could not be separated.

Both sex and daycare attendance were significantly associated with rhinovirus infection. Girls attending daycare had a much higher rate of rhinovirus infection (169) than did boy daycare attenders (50) or all infants not in daycare (48). In addition, 54% of girl daycare attenders had multiple infections compared with 20% of the boys: 77% of girls in daycare had had at least one infection compared with 53% for all infants combined.

Seventy four per cent of low socioeconomic class infants had had at least one para 3 infection compared with 47% for medium socioeconomic class and 54% for high, and this is reflected in the trend (not significant) in overall infection rates. None of the viruses considered was significantly associated with parental smoking for 1976-80. A significant relationship was found only for RSV and smoking mothers at home ( $p=0.020$ ) when 1975-6 data were included.



Evidence of respiratory syncytial, parainfluenza type 3, and influenza A and B virus infection in study infants, Houston Family Study 1975-80. Serological rise included failure of fall of passively acquired maternal antibody.

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Table 1. Virus infection rates per 100 child years for 131 infants according to sex, race, smoking. Number of siblings and daycare: Houston Family Study, 1976-80.

Virus	Sex		Race		Socioeconomic class				Parental smoking				No. of siblings				Daycare	
	Male		Female		Low		Medium		Yes		No		0		1		Yes	
	(n=47)	(n=45)	(n=59)	(n=33)	(n=23)	(n=48)	(n=21)	(n=48)	(n=37)	(n=33)	(n=37)	(n=34)	(n=37)	(n=37)	(n=37)	(n=34)	(n=31)	(n=49)
Respiratory syncytial virus	64	84	73	76	74	76	73	76	73	71	73	79	69	69	70	70	73	73
Parainfluenza type 3	70	80	57	70	87	56	57	70	60	63	63	63	63	63	63	63	63	63
Influenza A and B	26	34	17	39	23	19	23	23	23	27	11	34	31	31	22	22	24	24
Parainfluenza types 1 and 2	10	13	12	12	9	14	12	13	13	11	9	21	13	13	17	17	10	10
Adenovirus	20	24	22	20	26	23	23	23	23	21	14	23	23	23	23	23	23	23
Parainfluenza unidentified	26	29	25	21	21	24	25	24	24	23	24	27	13	13	13	13	24	24
Rhinovirus	44	84	61	70	34	67	64	69	74	48	76	72	72	72	72	72	72	72
Enterovirus	62	50	59	61	56	43	50	46	69	57	57	59	63	63	63	63	64	64
Total virus infection	340	376	334	379	404	332	333	334	346	372	413	367	404	404	404	404	404	404

$\chi^2 = 0.33$ ,  $p = 0.074$ .

$\chi^2 = 1.1$ ,  $p = 0.29$ ,  $p = 0.012$ .

$\chi^2 = 2.17$ ,  $p = 0.14$ ,  $p = 0.017$ ,  $p = 0.043$ .

$\chi^2 = 2.45$ ,  $p = 0.023$ .

$\chi^2 = 1.05$ ,  $p = 0.07$ .

$\chi^2 = 1.04$ ,  $p = 0.07$ .

Table 2. Respiratory illness rates per 100 child years for 131 infants according to sex, race, smoking, number of siblings, and daycare: Houston Family Study 1976-80.

Illness	Sex		Race		Socioeconomic class				Parental smoking				No. of siblings				Daycare	
	Male		Female		Low		Med		Yes		No		0		1		Yes	
	(n=47)	(n=45)	(n=59)	(n=33)	(n=23)	(n=48)	(n=21)	(n=48)	(n=37)	(n=33)	(n=37)	(n=34)	(n=37)	(n=37)	(n=37)	(n=34)	(n=31)	(n=49)
Allergic URI	340	340	344	343	600	523	334	343	343	343	343	343	343	343	343	343	343	343
Parainfluenza	166	166	169	168	165	160	150	157	167	167	167	167	167	167	167	167	167	167
Cold and flu	70	46	66	54	82	32	34	63	63	63	63	63	63	63	63	63	63	63
Total URI	705	707	701	700	847	770	762	787	787	787	787	787	787	787	787	787	787	787
LTD	63	42	54	42	70	71	31	31	31	31	31	31	31	31	31	31	31	31
Respiratory	45	20	39	39	34	20	39	39	39	39	39	39	39	39	39	39	39	39
Pneumonia	3	9	3	9	6	9	3	3	3	3	3	3	3	3	3	3	3	3
Total LTD	109	83	100	90	140	100	72	72	72	72	72	72	72	72	72	72	72	72
Total respiratory illness	895	870	861	820	990	870	834	871	871	871	871	871	871	871	871	871	871	871

$\chi^2 = 11.30$ ,  $p = 0.003$ , low = high  $p = 0.006$ , med = high  $p = 0.042$ .

$\chi^2 = 10.67$ ,  $p = 0.012$ .

$\chi^2 = 10.67$ ,  $p = 0.012$ .

URI = Upper respiratory illness.

LTD = Lower respiratory illness.

LTD = Lower respiratory illness.

Table 1 shows that influenza A and B infection rates varied significantly with race. Data for 1975-6 influenza A and B infections were combined with the 1976-80 data because surveillance of the influenza A/Victoria epidemic that occurred was comparable with later years (table 3). The significant association

with race was also seen in 1975-80. In addition, significant associations were found for race and influenza A only ( $p = 0.008$ ). Seventy three percent of these black infants had one or more siblings (1975-80) compared with 56% of white, but for 1976-80 this was reversed (black 41% white 53%).

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Table 3 Influenza A and B infection rate per 100 child years according to selected social and family factors, 1975-80

	No	Influenza A & B infection rate
Sex: Boy	67	27
Girl	64	24
Race: White	72	19
Other	89	44*
Socioeconomic class:		
Low	61	41
Medium	22	18
High	46	22
Parental smoking:		
Yes	66	33
No	63	27
No of siblings:		
0	49	18
1	41	32
≥2	41	44†
Daycare:		
Yes	36	33
No	101	20

\* $\chi^2=8.14$ ,  $p=0.004$ , influenza A only,  $p=0.034$  black v white,  $p=0.008$ .

† $\chi^2=6.97$ ,  $p=0.030$ , influenza A only,  $p=0.013$  0 v ≥2,  $p=0.008$ .

Influenza A and B infection was also significantly related to number of siblings as was influenza A alone ( $p=0.013$ ). A stronger association was seen when comparing none with two or more siblings ( $p=0.008$ ). These relationships with number of siblings were not seen with the 1976-80 data only.

Independence between race and number of siblings for low socioeconomic infants was suggested by analysing all three factors simultaneously. There was a trend towards increase in the rate of infection with number of siblings for both white and non-white in the low socioeconomic group; non-white infants had higher rates compared with white in each sibling category. This was not seen in any other socioeconomic group or for the data as whole. Most influenza A and B infections (25/40), however, occurred in the low socioeconomic infants (mostly due to the A/Victoria epidemic of 1975-6) and numbers were too small in other comparisons. Regardless of how the data were grouped, all analyses comparing infants with no siblings with infants with one or two or more siblings showed lower rates of infection in those without siblings. In addition to the association with number of siblings, 70% of infants with two or more siblings had at least one school aged sibling, whereas for those with only one, the sibling tended to be of preschool age (15% school aged). During the epidemic of 1975-6, 38% of

the study infants had evidence of infection and 80% of these had school age siblings.

#### RESPIRATORY ILLNESS

Respiratory illness rates are shown in table 2 according to the selected social and family factors. In general, the significant relationships and interesting trends found were in the area of more severe illness. As shown in the first two columns of table 2, boys had higher rates of illness in several of the diagnostic categories but none of these trends was significant. The rate of total LRD varied significantly with both socioeconomic class (low v high only) and daycare attendance, and a similar trend was noted with increasing number of siblings. There were indications that all three factors may affect total LRD independently. The larger families were distributed almost equally among all three socioeconomic classes, although low and medium classes had higher percentages of families with two or more siblings (low 39%, medium 38%, high 19%). Rates of total LRD for infants with two or more siblings were found to be highest in low socioeconomic families (166 per 100 child years) and lowest in high socioeconomic class families (80 per 100 child years). Also the low socioeconomic families were the least likely to send their infants to daycare. Only 13% of low socioeconomic infants were in daycare compared with 28% of the medium and 35% of the high socioeconomic class infants.

Rates of total LRD for girls and boys not attending daycare were 69 and 105, respectively, while girl and boy infants attending daycare had rates of 123 and 120. Rates of bronchiolitis and pneumonia were essentially equal for both sexes in daycare.

A statistically significant variation in the rate of LTB (a component of LRD) was also found in all three socioeconomic classes, but separate analysis of medium v high was found not to be significant ( $p=0.062$ ).

No statistically significant relationship was seen between total respiratory illness and parental smoking for the 1976-80 infants. Nevertheless, data on severe illnesses in 1975-6 were comparable with later years, and all six episodes of pneumonia that year occurred in infants of mothers who smoked. Overall, from 1975 to 1980 there were 11 episodes of pneumonia and nine (82%) occurred in black infants of mothers who smoked. The highest rate of pneumonia (25) was found in infants with non-employed mothers who smoked and this compared with a rate of 1.5 in those with non-employed mothers who were non-smokers ( $p=0.001$ ).

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### Discussion

In this study we closely monitored infants for viral infections and respiratory symptoms through the first year of life for five consecutive years. Since we studied proved viral infection regardless of illness and all illnesses regardless of severity, differences in groups based on family recognition of illness and patterns of medical care were minimised. It might therefore be expected that for such a ubiquitous group of viruses and such common illnesses the impact of family and social factors would not be impressive. In fact, we were unable to find any consistent overall relationship between respiratory viral infection or illness and the social factors studied. We had previously noted a similar lack of overall effect of breast feeding on viral respiratory infection and illness in this same population.<sup>10</sup> Within this general similarity of experience among infants living under different conditions, however, there were selected findings of interest, especially in relation to previous reports. This group of observations will be summarised and then discussed individually. RSV and para 3 notably could not be confidently related to any of the study factors. The infection rates of rhino, influenza, and adenoviruses were all significantly associated with two of the study factors but the strongest and clearest relationships were found for influenza viruses. Respiratory illness varied significantly with the study factors only when looking at more serious illness categories. Important trends included variation in severe illness rates with sex and number of siblings while significant relationships existed between LRD, socioeconomic class, and daycare. No differences in LRD were found in relation to parental smoking as an isolated factor.

RSV is a major cause of respiratory illness in young children, especially bronchiolitis and pneumonia.<sup>11-13</sup> Previous studies have found no correlation between RSV infection and sex, race, or socioeconomic class<sup>11-13</sup> although sex, low socioeconomic class, and number of siblings, may influence the outcome of infection.<sup>14-16</sup> Our data also show no correlation between RSV infection and sex, race, or socioeconomic class, and, in addition, we found no association with daycare. The relationship to parental smoking must be considered questionable because of the limitations of the data relative to this virus in 1975-6. Hall *et al* also found a questionable relationship between parental smoking and RSV infection so that any association continues to be undocumented.<sup>16</sup> Sixty nine per cent of our study infants had had at least one RSV infection; this shows the high incidence in this age group.

Parainfluenza type 3 virus is also a major cause of LTB in young children and is an important cause of

bronchiolitis and pneumonia in infants and children,<sup>17</sup> but the influence of social and family factors have been little studied. Our results show a higher incidence of initial infections among infants of low socioeconomic class but no significant association with any of the factors studied. Fifty five per cent of the infants had had at least one parainfluenza 3 virus infection.

Our study indicates that for influenza viruses (particularly type A) both race and number of siblings influence the rate of infection. Kim *et al* found that a larger percentage of black infants (especially boys) in hospital for respiratory illness during 11 influenza epidemics had influenza A virus infection,<sup>18</sup> and our very different approach also gave indications that blacks are at a greater risk for influenza A infection. The effect of race on influenza infection was not influenced by family size or socioeconomic class even though a larger number of non-whites were in the low socioeconomic class. The present data also point to older siblings, particularly school age children, as introducers; infants were more likely to be infected if they had school aged siblings in the home. This was especially true during the epidemic of 1975-6 as previously reported<sup>7</sup> and has been observed by others.<sup>19</sup> Hall *et al* found that preschoolers were more often responsible for spread of infection within the family based on age-specific infection rates, but they noted that infection rates based on a fourfold serological rise rather than the twofold rise they used would have shifted the highest age-specific infection rates to school age children.<sup>20</sup> Rhinovirus infection rates were found to be influenced by sex and daycare attendance. In both instances the reason appeared to be a high rate of infection in girls attending daycare for which we have no explanation.

Variation in illness with social and family factors was generally restricted to LRD rates and most of the findings reported previously also refer to LRD. Boys have been shown to have higher rates of LRD compared with girls<sup>6-8, 11-13</sup> at least to the age of 6. Although we found that the difference between boys and girls was not significant for LRD, the ratio of illness, especially when looking only at non-daycare attenders, was very close to the 60:40 ratio found by Gardner.<sup>6</sup> The presence of siblings has also been shown by previous studies to affect the seriousness and number of illnesses.<sup>6-8</sup> We were unable to show that the difference in illness rates between number of siblings was significant for LRD but the trend was very suggestive.

Low socioeconomic status has been thought to influence the rate of respiratory illness by means of overcrowding, large family size, and inadequate medical care.<sup>6-8</sup> We provided uniform medical care

and still found a higher rate of LRD among infants of low socioeconomic class even when controlled for family size (although numbers were small) and despite the fact that few of these infants were in daycare. Factors other than medical care or family size seem to be important influences on the incidence of LRD in the low socioeconomic infants. Trends to more infection and illness in general were present in this group.

Past studies have implicated daycare attendance as a cause of increased respiratory illness in children, especially infants. Strangert and Loda *et al* noted this in infants aged 6–15 months and under 12 months old, respectively.<sup>17,18</sup> Vihma found annual illness rates in daycare compared with home to be 6.3 v 2.5.<sup>19</sup> These results are in agreement with our findings. In addition, we found that girl infants in daycare seem to lose the relative "protection" from LRD observed for girl infants at home. Rates of serious lower respiratory disease—that is, bronchiolitis and pneumonia—were equal in boy and girl daycare attenders.

Infants of parents who smoked in our study were not at greater risk for viral infection or respiratory illness and even had a lower rate of LTB. The only exception to this was a significant relationship between pneumonia and parental smoking (especially mothers at home who smoked) only evident when the 1975–6 data were included. This effect could not be separated from the influence of race or socioeconomic class. Our observations are in contrast with those of Harlap and Davies<sup>20</sup> and Leeder *et al*.<sup>9</sup> Both studies found a highly significant relationship between passive smoking and lower respiratory illness, specifically bronchitis and pneumonia. Methods in these studies differed considerably from our own; Harlap and Davies used data from large numbers of infants in hospital whereas Leeder *et al* followed up a cohort of children by means of yearly questionnaires. Although the total number of episodes of LRD (112 including 1975) experienced by the infants in our study was small by comparison (especially pneumonia), ascertainment was more direct and illnesses were well documented.

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Harrington, W., Krupnick, A.J. "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children" J Air Pollut Control Assoc 35: 1061-1067, 1985.

ABSTRACT. A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between NO<sub>2</sub> ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and NO<sub>2</sub> concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

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# Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children

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A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between  $\text{NO}_2$  ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and  $\text{NO}_2$  concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

Since the passage of the Clean Air Act in 1970, several epidemiological studies have attempted to associate morbidity with indoor and outdoor exposure to nitrogen dioxide ( $\text{NO}_2$ ). The indoor, so-called gas stove studies<sup>1-7</sup> produced mixed and inconclusive results in their attempts to link health impairment to the presence of a gas stove or gas heater in the home. Studies of the health effects of outdoor  $\text{NO}_2$  exposures also have failed to find consistently significant health effects at ambient exposure levels.<sup>8-11</sup>

In an analysis of people living in Chattanooga, Tennessee, conducted under the Community Health and Environmental Surveillance System (CHES) program, Shy and Love<sup>12</sup> were able to link  $\text{NO}_2$  exposures and acute respiratory disease. However, several problems have been raised about this study. The researchers have been criticized for using rudimentary statistical techniques, consisting mainly of pairwise comparison of illness incidence rates in subpopulations. In addition, the data base has been tainted by its association with the controversial CHES program.<sup>13</sup> [The earlier CHES Chattanooga studies were also criticized for using a subsequently discredited method (Jacobs-Hochheiser) for monitoring  $\text{NO}_2$  concentrations. However, by 1972 the Saltzman technique was being used.] Yet EPA has found the Chattanooga data to be accurately transferred from the surveys to the computer tapes and our own research has revealed the data quality to be at least as high as other similar, but much less controversial data bases.

The lack of persuasive epidemiological studies upon which to base a national ambient air quality standard for nitrogen dioxide motivated the present paper. Here we return to the CHES aerometric and health data bases collected during

1972-73 in Chattanooga and used by Shy and Love to examine the relationship between  $\text{NO}_2$  and acute respiratory disease in children. We first describe and defend the CHES-Chattanooga data base and the statistical model used to examine it. We then present our results and discuss a number of econometric issues and their relationship to our findings.

## The Data Base

In January 1972, a self-administered survey on chronic respiratory disease (CRD) was distributed to families with children in elementary schools in one of the three Chattanooga communities, Harrison, Brainerd, and Redbank, located within one mile of an air pollution monitoring station. A subsample of families—1970 parents and their children, 4898 individuals in all—was drawn from this sample to participate in an acute respiratory disease (ARD) panel survey. Information was taken in two-week intervals (always beginning on a Sunday) over three school semesters from spring 1972 through spring 1973. Each family was phoned within several days after the end of each two-week period to determine if any family members experienced various acute respiratory disease symptoms or consulted a physician.

Aerometric data were gathered at seven sites. Hourly measurements of  $\text{NO}_2$  were taken using the Saltzman chemiluminescence technique only for the fall 1972 and spring 1973 study periods. Thus, we eliminated data for the spring 1972 period from our analysis. Chattanooga was chosen as a site for an  $\text{NO}_2$  study because it featured a TNT plant emitting large quantities of nitrogen-based pollutants. This plant closed January 1, 1973, resulting in reduced  $\text{NO}_2$  concentrations in the nearby communities. Daily readings were taken on particulates, nitrates, and sulfates. These daily readings were reduced to monthly frequency distributions. Unfortunately, the original daily data were unavailable from EPA, and we have been forced to use the monthly frequency distributions for the latter three pollutants.

The Chattanooga health and aerometric data collection effort of the early 1970s and the CHES program in general have been criticized (Roth<sup>14</sup>) for their poor survey protocols, health data inconsistencies, and aerometric data unreliability. Krupnick and Harrington<sup>15</sup> provide a complete reanalysis of these data and find, first, that the survey protocols were carefully designed and observed. In addition, responses to identical sociodemographic questions on the CRD and ARD surveys were found to be quite consistent. Also, the  $\text{NO}_2$  monitoring data were found to be reasonably complete, generally consistent, and taken by devices that generally outperform other types of monitors in the lab.

Further, because a duplicate CRD survey was administered to some of the participants 22 months later, we were

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able to identify inconsistencies intertemporally. Drawing on responses from 948 parents and considering only the questions concerning age, race, birthdate, education, and smoking status, over 80% of the parents had matching responses over the two surveys. These results compare favorably to similar investigations of the U.S. Census and other highly regarded data bases.<sup>14,17</sup>

In the course of our examination of the quality of this data base we noted a number of recall-related problems inherent in the survey procedure. These problems may also be present in parts of other surveys, such as the Health Interview Survey (HIS), that rely on biweekly interviews to collect acute respiratory disease data. These problems are discussed in some detail elsewhere,<sup>18</sup> but the main points may be summarized as follows:

1) Respondents have imperfect recall of the day or even week of onset of illness. For example, over 60% of illnesses reported were said to have occurred in the second week of the recall period, a result significantly ( $\alpha = 0.01$ ) different from the uniform distribution one would expect. Apparently respondents either forget (presumably minor) illnesses occurring in the first week, or they remember disease onset as occurring later than was actually the case.

2) When average duration of reported illness is plotted as a function of day of onset during the two-week period, a linear decline is found during the second week of the period, with average duration at the end of the week barely half of average duration at the beginning. The most likely explanation is that illnesses extending past the end of the period are not reported accurately, even though interviewers were instructed to identify such illnesses and ask about them at the end of the next reporting period. If this explanation is correct, the truncation of restricted activity days imparts a downward bias to illness severity.

3) In other panel studies it has been suggested that respondents may, over time, progressively under-report illness simply because they become tired of doing interviews. If pollution levels are time-dependent, the study results may be biased accordingly. We found little evidence of this phenomenon. On the assumption that less serious illnesses could

Table II. Pollution statistics.

	Mean ( $\mu\text{g}/\text{m}^3$ )	Standard deviation	Correlation coefficients		
			PAR90P	SUL90P	TEMP
NO2MAX	98.0	48.3	-0.10	0.20	-0.09
PAR90P	100.6	31.4		-0.027	0.34
SUL90P	10.0	2.7			-0.036

be more likely to be neglected, we regressed the ratio of "serious" to total illness incidence on time, and found no trend.

These findings affected our subsequent data analysis in two ways. First, no attempt was made to use time intervals shorter than two weeks, even though the sample could be reduced to weekly or even daily observations. Second, we concentrated on the incidence of illness rather than duration, inasmuch as we felt the former to be more reliable.

#### The Model

To identify the factors affecting reported children's disease, we use pooled cross-section time series models predicting illness incidence or duration as a function of demographic, pollution, and weather variables. Symbolically, the models are of the form

$$S_{ijt} = f(X_{ij}, P_{jt}, W_t) + \epsilon_{ijt}$$

where  $S_{ijt}$  is the reported incidence or duration of the illness of the  $i$ th child in the  $j$ th neighborhood during period  $t$ ,

$X_{ij}$  is a vector of personal variables for the  $i$ th child in the  $j$ th neighborhood,

$P_{jt}$  is a vector of pollution variables for the  $j$ th neighborhood in period  $t$ ,

$W_t$  is the weather in period  $t$ , and

$\epsilon_{ijt}$  is the disturbance term.

The independent variables are defined as follows:

AGE:	the child's age at the beginning of the school year.
RACE1W:	the race of the head of household; 1 if white, 0 if nonwhite.
CHESTINF:	1 if the child has suffered a respiratory infection within the past three years, 0 otherwise.
CHRON:	1 if the child suffers from asthma or a chronic heart or lung condition, 0 otherwise.
EDU:	the years of schooling completed by the head of household.
MOMHEAD:	1 if the household head is female, 0 otherwise.
SMKPPD:	mother's smoking in packs per day.
CROWD:	number of household members divided by the number of rooms in the house.
SEX1F:	sex of child; 1 if female, 0 if male.
GAS:	1 if the kitchen stove is gas, 0 if electric.
RAIN:	amount of rainfall during the period, in inches.
EPIDEM:	monthly influenza cases reported by the State of Tennessee (in thousands).
TEMP:	the absolute difference between the average temperature during the period and 65°.
NO2MAX:	average daily maximum concentration of $\text{NO}_2$ , in $\mu\text{g}/\text{m}^3$ .
PAR90P:	90th percentile total suspended particulate concentration during the month, in $\mu\text{g}/\text{m}^3$ .
SUL90P:	90th percentile sulfate concentration during the month, in $\mu\text{g}/\text{m}^3$ .

As noted above, two dependent variables are considered: illness incidence (NEWILL), which is 0 or 1 according to

Table I. Descriptive statistics ( $N = 2093$ ).

Variable	Mean value or population fraction
NEWILL	0.13
RADS	0.21
AGE	7.7
Age distribution	
0-2	0.09
3-4	0.06
5-6	0.16
7-8	0.23
9-10	0.25
11-12	0.19
RACE1W	0.91
CHESTINF	0.28
CHRON	0.07
Education of household head	
High school graduate	0.71
Attended some college	0.45
MOMHEAD	0.05
Mothers' smoking status	
Current	0.32
Ex-	0.15
Non-	0.53
CROWD	1.30
SEX1F	0.48
GAS	0.05
RAIN	2.70
TEMP	18.20

Table III. Predicting illness incidence in population subsamples.<sup>a</sup>

	A	B	C	D	E	F	G	H	I
	All children 12 and under	Children with nonsmoking mothers	Children with smoking mothers	Children without chronic respiratory disease	Children with CRD	Children 6 and under	Infants	Fall only	Spring only
Intercept	0.0512 (0.0503)	0.064 (0.059)	-0.0197 (0.091)	0.052 (0.056)	0.098 (0.095)	0.037 (0.10)	0.151 (0.21)	0.161 (0.113)	0.018 (0.075)
NO2MAXL	-8.87E-4 (2.05E-4) <sup>c</sup>	-6.10E-4 (2.46E-4) <sup>b</sup>	-13.5E-4 (3.71E-4) <sup>c</sup>	-6.4E-4 (2.3E-4) <sup>c</sup>	-13.6E-4 (4.0E-4) <sup>c</sup>	-8.44E-4 (4.1E-4) <sup>b</sup>	-12.5E-4 (8.7E-4)	0.26E-4 (4.3E-4)	-15.0E-4 (2.9E-4) <sup>c</sup>
NO2MAXH	1.71E-4 (0.68E-4) <sup>b</sup>	2.19E-4 (0.78E-4) <sup>c</sup>	-5.7E-4 (1.46E-4)	2.3E-4 (1.13E-4) <sup>b</sup>	5.1E-4 (1.34E-4)	2.41E-4 (1.89E-4)	5.2E-4 (2.55E-4) <sup>b</sup>	0.06E-4 (0.78E-4)	3.95E-4 (2.01E-4) <sup>b</sup>
PAR90P	8.88E-4 (6.08E-4)	6.69E-4 (7.4E-4)	14.3E-4 (10.8E-4)	11.4E-4 (6.8E-4)	4.00E-4 (12E-4)	12.1E-4 (11.9E-4)	13.0E-4 (24E-4)	28.1E-4 (15E-4)	13.4E-4 (9.1E-4)
PAR90P2	-0.053E-4 (0.028E-4) <sup>c</sup>	-0.044E-4 (0.03E-4)	-0.075E-4 (0.048E-4)	-0.056E-4 (0.031E-4)	-0.041E-4 (0.055)	-0.066E-4 (0.064)	0.045E-4 (0.11E-4)	-0.146E-4 (0.074E-4)	-0.056E-4 (0.039E-4)
SUL90P	135E-4 (45.9E-4) <sup>c</sup>	117E-4 (54E-4) <sup>b</sup>	191E-4 (87E-4) <sup>b</sup>	89.8E-4 (53E-4)	231E-4 (87.8E-4) <sup>c</sup>	128E-4 (90E-4)	219E-4 (195E-4)	-156E-4 (217E-4)	85.3E-4 (65.7E-4)
SUL90P2	-5.54E-4 (1.72E-4) <sup>c</sup>	-4.81E-4 (2.0E-4) <sup>b</sup>	-7.91E-4 (3.32E-4) <sup>b</sup>	-3.67E-4 (1.97E-4)	-9.36E-4 (3.24E-4) <sup>c</sup>	-5.46E-4 (3.3E-4)	-11.6E-4 (7.5E-4)	5.76E-4 (9.9E-4)	-3.38E-4 (2.2E-4)
AGE	-0.0185 (0.0034) <sup>c</sup>	-0.0165 (0.0042) <sup>c</sup>	-0.0252 (0.0057) <sup>c</sup>	-0.022 (0.0071)	-0.010 (0.0071)	d	e	-0.0207 (0.0047) <sup>c</sup>	-0.0164 (0.0048) <sup>c</sup>
AGE2	7.53E-4 (2.44E-4) <sup>c</sup>	5.14E-4 (3.0E-4)	14.9E-4 (4.2E-4) <sup>c</sup>	8.99E-4 (2.66E-4) <sup>c</sup>	3.32E-4 (5.27E-4)	d	e	8.71E-4 (3.47E-4) <sup>c</sup>	6.4E-4 (3.46E-4)
CHESTINF	0.0475 (0.010) <sup>c</sup>	0.0495 (0.012) <sup>c</sup>	0.044 (0.018) <sup>c</sup>	0.044 (0.011) <sup>c</sup>		0.071 (0.019) <sup>c</sup>	0.103 (0.042) <sup>b</sup>	0.046 (0.014) <sup>c</sup>	0.048 (0.015) <sup>c</sup>
CHRON	0.044 (0.0059) <sup>c</sup>	0.0390 (0.0071) <sup>c</sup>	0.052 (0.011) <sup>c</sup>			0.036 (0.011) <sup>c</sup>	0.003 (0.024)	0.036 (0.0083) <sup>c</sup>	0.052 (0.0084) <sup>c</sup>
CROWD	0.0184 (0.0073) <sup>b</sup>	0.0163 (0.0090)	0.018 (0.013)	0.019 (0.0083) <sup>b</sup>	0.011 (0.014)	0.037 (0.017) <sup>b</sup>	0.029 (0.715)	0.022 (0.010) <sup>b</sup>	0.0156 (0.010)
EDU	-0.0012 (0.0021)	-0.0045 (0.0028)	0.0056 (0.0039)	-0.0016 (0.0025)	-0.0060 (0.0095)	-0.0029 (0.0046)	-0.0031 (-0.315)	-0.00028 (0.0031)	-0.0024 (0.0032)
EPIDEM	0.072 (0.011) <sup>c</sup>	0.089 (0.013) <sup>c</sup>	0.036 (0.019)	0.055 (0.012) <sup>c</sup>	0.099 (0.021) <sup>c</sup>	0.064 (0.022) <sup>c</sup>	0.059 (1.31)	-0.23 (0.085) <sup>c</sup>	0.098 (0.017) <sup>c</sup>
SEX1F	0.0076 (0.0052)	0.0083 (0.0063)	0.006 (0.0092)	0.0066 (0.0058)	0.011 (0.010)	-0.0080 (0.011)	0.0027 (0.023)	0.0021 (0.0072)	0.012 (0.0071)
SMKPPD	-0.0013 (0.0020)		0.0019 (0.0049)	-0.0027 (0.0023)	0.0021 (0.0036)	-0.0050 (0.0040)	-0.0058 (0.0086)	0.00126 (0.0028)	-0.0037 (0.0028)
GAS	-0.020 (0.012)	-0.044 (0.015) <sup>c</sup>	0.012 (0.019)	0.0044 (0.014)	-0.061 (0.021) <sup>c</sup>	-0.057 (0.026) <sup>b</sup>	-0.070 (0.061)	-0.0012 (0.016)	-0.036 (0.016) <sup>b</sup>
RAIN	-0.0056 (0.0016) <sup>c</sup>	-0.0068 (0.0019) <sup>c</sup>	-0.0027 (0.0027)	-0.0050 (0.0017) <sup>c</sup>	-0.0060 (0.0031)	-0.0054 (0.0032)	0.0019 (0.0064)	-0.019 (0.0053) <sup>c</sup>	-0.0027 (0.0020)
TEMP	0.0022 (0.00040) <sup>c</sup>	0.0021 (0.00048) <sup>c</sup>	0.0025 (0.00072) <sup>c</sup>	0.0020 (0.00045) <sup>c</sup>	0.0026 (0.00081) <sup>c</sup>	0.0029 (0.00082) <sup>c</sup>	0.0015 (0.0018)	0.0018 (0.00086) <sup>b</sup>	0.0026 (0.00066) <sup>c</sup>
RACE1W	0.056 (0.0090) <sup>c</sup>	0.039 (0.012) <sup>c</sup>	0.073 (0.14) <sup>c</sup>	0.051 (0.0095) <sup>c</sup>	0.060 (0.019) <sup>c</sup>	0.059 (0.017) <sup>c</sup>	0.087 (0.039) <sup>b</sup>	0.034 (0.013) <sup>c</sup>	0.075 (0.013) <sup>c</sup>
N	16474	11497	4977	11557	5246	5108	1387	8176	8298
F	25.5	19.7	8.83	15.29	8.33	5.68	1.84	8.37	22.5
R <sup>2</sup>	0.0286	0.030	0.033	0.022	0.026	0.027	0.025	0.019	0.049

<sup>a</sup> Standard errors in parentheses.<sup>b</sup> Significant at the 5% level.<sup>c</sup> Significant at the 1% level.<sup>d</sup> AGE and AGE2 were replaced by dummy variables AGEONE (= 1 if AGE = 1, 0 otherwise) and AGETWO.<sup>e</sup> AGE and AGE2 were replaced by dummy variables AGEONE through AGESIX.

whether the child is reported ill during the two-week period in question, and duration of restricted activity (RADS), which takes an integer value between 0 and 14.

Tables I and II provide descriptive statistics on these variables. Note the low number for mean RADS, indicating the large percentage of observations with a zero value for this variable. Correlation coefficients between each of the pollutants and temperature are also provided. Note that correlations between pollutants are all quite low. We searched for more complicated patterns of collinearity by using the diagnostic tests<sup>18</sup> provided with the SAS regression package. These tests failed to reveal any serious collinearity problems involving any of the independent variables.

We relied primarily on a linear probability model for our analysis, using ordinary least squares (OLS) as the estimation procedure, the results of which are presented below. However, the OLS model requires a number of assumptions of questionable validity for the current problem. We discuss later the effects of these assumptions on the outcomes.

## Results

Table III shows the results of the regressions predicting illness incidence. Column A gives the results for the entire sample of children aged 12 and under. The remaining columns show results for a number of subpopulations; we used these results to examine the stability of the coefficients and to identify populations especially sensitive to the pollution variables. Thus, Columns B and C give results for children of mothers who do and do not smoke, and Columns D and E give results for children with and without chronic respiratory disease or a history of respiratory ailments. In Columns F and G we examine the illness incidence in younger children. Finally, in Columns H and I we divide the sample into fall (October–December 1972) and spring (January–April 1973) time periods.

The specification of the NO<sub>2</sub> variable was piecewise linear, with a break at 100 µg/m<sup>3</sup>. This specification was the best of all those examined. In Table III NO2MAXL and NO-

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2MAXH refer, respectively, to average daily maximum concentrations below and above  $100 \mu\text{g}/\text{m}^3$ . As shown, for NO<sub>2</sub>MAX concentrations below  $100 \mu\text{g}/\text{m}^3$ , illness probability falls relatively sharply as NO<sub>2</sub>MAX increases. Above  $100 \mu\text{g}/\text{m}^3$  illness probability gradually increases with NO<sub>2</sub>MAX, but the illness rate at the highest observed two-week maximum concentration ( $384 \mu\text{g}/\text{m}^3$ ) is less than that at the lowest observed concentration ( $27 \mu\text{g}/\text{m}^3$ ). The clinical literature gives no reason why a dose-response function should have these characteristics.

In the subsamples (Columns B to I), the above relationship between NO<sub>2</sub>MAX and illness is replicated for children with nonsmoking mothers and children without a history of respiratory disease. For both preschool age children and infants, the coefficients were similar although not always significant. However, for children whose mothers smoke or have a chronic respiratory condition, NO<sub>2</sub>MAXH has virtually no effect. Finally, when only fall periods are examined, NO<sub>2</sub>MAX is not related to illness at all.

These exceptions did not increase our confidence in the results. The first two exceptions suggest that a "sensitive population" for NO<sub>2</sub> is healthy older children of nonsmoking mothers. If so, perhaps the presence of a chronic condition swamps the small NO<sub>2</sub> effect. Likewise, perhaps for children exposed to parental smoking an additional NO<sub>2</sub> effect cannot be detected. One problem with this explanation is that we found no adverse effect of mother's smoking on children's health. As for the absence of an NO<sub>2</sub> effect in the fall, we note that the prevalence of illness in that season was relatively low in any event. If the effect of NO<sub>2</sub> is to reduce resistance to disease, we might expect to find no NO<sub>2</sub> effect when little disease is present in the community. Such speculation notwithstanding, we have not found an effect from NO<sub>2</sub> that is supported by clinical evidence or that is present in all population subgroups.

For sulfates and particulates the best fits were obtained for the 90th percentile of two-week concentration and a quadratic specification, with a positive linear and negative square term. The particulate results were reasonably consis-

tent across subpopulations, but rarely significant at the 5% level. Moreover, the various functions were such that the effects of particulates on illness were negative at concentrations below  $80\text{--}100 \mu\text{g}/\text{m}^3$ , which is near the average 90th percentile concentration. That is, over much of the relevant range the particulate variable is inversely related to illness.

The coefficients for sulfates are significant for the entire sample, but not for the fall and spring semesters separately. For fall, the coefficients enter with signs and reverse of all other subsamples, but the *t*-values are very small. For spring, the coefficients are similar to coefficients in other equations but the *t*-values still are not significant. For the population subsamples the sulfate coefficients are stable and significant except for infants, where, as we have noted, sample sizes are much smaller and an effect of population on health would be correspondingly more difficult to identify. The inconsistent seasonal results may be related to using weighted averages of monthly summaries of daily readings instead of two-week averages, which were unavailable for particulates and sulfates.

Turning briefly to the other explanatory variables, the most statistically significant and robust results were for variables that one would expect to be associated with respiratory disease: age, a history of chest infection, presence of a chronic condition, the extent of crowding in the home, and outside temperature. Not only were these variables almost always significant, but the coefficients were stable across subpopulations. The coefficients for CHRON (presence of chronic disease), for example, varied between 0.036 and 0.052, except in the equation for infants, and indeed very few infants in the sample were diagnosed for a chronic disease. The EPIDEM variable was also generally significant but in the fall the sign was negative, a result we believe to be fortuitous, inasmuch as the variable was very small in absolute value during that season.

For two other variables, RACE1W and RAIN, the results were stable and significant. White children consistently reported more new illness than nonwhites. We also found a consistent inverse relationship between the amount of rain-

Table IV. Comparison of specifications of NO<sub>2</sub> variables in equations predicting illness incidence.\*

	A	B	C	D	E	F	G
NO <sub>2</sub> MAX	1.4E-6 (56.8E-6)	-3.5E-4 (1.82E-4) <sup>b</sup>	-21.7E-4 (4.37E-4) <sup>c</sup>				
NO <sub>2</sub> MAX2		0.009E-4 (0.0045E-4)	11.3E-6 (2.31E-6) <sup>c</sup>				
NO <sub>2</sub> MAX3			-1.59E-8 (0.35E-8) <sup>c</sup>				
NO <sub>2</sub> MAX(0-75)				-19E-4 (4.63E-4) <sup>c</sup>	-21E-4 (4.88E-4) <sup>c</sup>		
NO <sub>2</sub> MAX(75-150)				-0.16E-4 (0.94E-4)			
NO <sub>2</sub> MAX(75-100)					-0.28E-4 (0.80E-4)		
NO <sub>2</sub> MAX(100-150)					1.2E-4 (1.1E-4)		
NO <sub>2</sub> MAX(>150)				1.7E-4 (1.15E-4)	0.56E-4 (1.19E-4)		
NO <sub>2</sub> MAX(0-100)						-8.9E-4 (2.05E-4) <sup>c</sup>	
NO <sub>2</sub> MAX(>100)						1.7E-4 (0.69E-4) <sup>b</sup>	
NO <sub>2</sub> AVG(0-50)							-9.4E-4 (4.1E-4) <sup>b</sup>
NO <sub>2</sub> AVG(>50)							1.96E-4 (3.8E-4)
F	25.8	24.7	24.5	24.0	23.2	25.5	24.7
R <sup>2</sup>	0.0274	0.0277	0.0289	0.0281	0.0288	0.0286	0.0278
N	16474	16474	16474	16474	16474	16474	16474

\* Standard errors in parentheses.

<sup>b</sup> Significant at the 5% level.

<sup>c</sup> Significant at the 1% level.

Table V. Cross section time series regression coefficients for illness incidence and restricted activity days: full sample vs. sample consisting of one child per family.\*

Variable	Illness incidence		Restricted activity days	
	Full sample	Sub-sample	Full sample	Sub-sample
Intercept	0.0512 (0.06)	-0.0016 (0.73)	0.348 (0.135) <sup>b</sup>	0.275 (0.20)
NO2MAXL	-8.87E-4 (2.05E-4) <sup>c</sup>	-7.98E-4 (2.9E-4) <sup>c</sup>	-25.0E-4 (5.6E-4) <sup>c</sup>	-28.7E-4 (8.3E-4) <sup>c</sup>
NO2MAXH	1.71E-4 (0.68E-4) <sup>b</sup>	1.39E-4 (0.99E-4)	4.4E-4 (1.86E-4) <sup>b</sup>	6.22E-4 (2.8E-4) <sup>b</sup>
PAR90P	8.88E-4 (6.08E-4)	17.8E-4 (8.8E-4) <sup>b</sup>	-18.3E-4 (16.6E-4)	9.80E-4 (24.5E-4)
PAR90P2	-0.053E-4 (0.028E-4)	-0.068E-4 (0.040E-4) <sup>b</sup>	0.064E-4 (0.075E-4)	-0.04E-4 (0.099)
SUL90P	135E-4 (45.9E-4) <sup>c</sup>	107E-4 (66E-4)	212E-4 (126E-4)	73.3E-4 (185E-4)
SUL90P2	-5.54E-4 (1.72E-4) <sup>c</sup>	-4.73E-4 (2.5E-4)	-9.3E-4 (4.7E-4) <sup>b</sup>	-4.26E-4 (6.9E-4)
AGE	-0.0185 (0.0034) <sup>c</sup>	-0.020 (0.0049) <sup>c</sup>	-0.045 (0.0092) <sup>c</sup>	-0.044 (0.014) <sup>c</sup>
AGE <sup>2</sup>	7.53E-4 (2.44E-4) <sup>c</sup>	8.54E-4 (3.6E-4) <sup>b</sup>	20.9E-4 (6.7E-4) <sup>c</sup>	19.1E-4 (10.0E-4)
CHESTINF	0.0475 (0.010) <sup>c</sup>	0.053 (0.015) <sup>c</sup>	0.178 (0.028) <sup>c</sup>	0.196 (0.042) <sup>c</sup>
CHRON	0.044 (0.0059) <sup>c</sup>	0.047 (0.0084) <sup>c</sup>	0.099 (0.016) <sup>c</sup>	0.110 (0.023) <sup>c</sup>
CROWD	0.0184 (0.0073) <sup>b</sup>	0.018 (0.010)	0.019 (0.020)	0.0080 (0.026)
EDU	-0.0012 (0.0021)	0.0028 (0.0032)	-0.0087 (0.0061)	-0.0023 (0.0088)
EPIDEM	0.072 (0.011) <sup>c</sup>	0.080 (0.015) <sup>c</sup>	0.228 (0.029) <sup>c</sup>	0.221 (0.042) <sup>c</sup>
SMKPPD	-0.0013 (0.0020)	-0.0039 (0.0028)	0.0004 (0.0050)	0.0086 (0.0078)
GAS	-0.020 (0.012)	-0.0021 (0.0016)	-0.037 (0.032)	0.0021 (0.045)
RAIN	-0.0056 (0.0016) <sup>c</sup>	-0.0049 (0.0022) <sup>b</sup>	-0.0037 (0.0043)	0.0025 (0.0061)
TEMP	0.0022 (0.0004) <sup>c</sup>	0.0020 (0.00057) <sup>c</sup>	0.0029 (0.0011) <sup>c</sup>	0.0030 (0.0016)
RACE1W	0.056 (0.0090) <sup>c</sup>	0.065 (0.014) <sup>c</sup>	0.127 (0.025) <sup>c</sup>	0.136 (0.038) <sup>c</sup>
SEX1F	0.0076 (0.0052)	0.0094 (0.0074)	0.023 (0.014)	-0.0039 (0.021)
N	16474	8158	16474	8158
F	25.5	13.6	20.5	10.6
R <sup>2</sup>	0.0286	0.031	0.023	0.024

\* Standard errors in parentheses.

<sup>b</sup> Significant at the 5% level.

<sup>c</sup> Significant at the 1% level.

fall and the incidence of illness in a two-week period, although the magnitude varied by a factor of six between fall and spring. Again, we have no explanation for this result. In addition, the presence of a gas stove in the house appeared to be unrelated to disease incidence. Few significant results were obtained, and for those that were significant the sign was contrary to expectation. As only 5% of the households cooked with gas, these generally inconsistent results are not particularly surprising.

Other covariates had virtually no explanatory power, and were rather unstable across subpopulations: educational level of head of household, sex, and mother's smoking status. In particular, we found that a mother's smoking in the home was unrelated to acute respiratory disease incidence of her children. However, this should not be too surprising in view of the contradictory findings on the health effects of passive smoking.<sup>19</sup>

An analysis was also carried out for illness duration as the dependent variable. In this case the dependent variable  $S_{ijt}$  took an integer value between 0 and 14. OLS estimates predicting illness duration were very similar to the results presented above; that is, independent variables that were

also significant and significant.

However, OLS estimates of truncated variables are inconsistent as well as inefficient,<sup>20</sup> so it is especially important to compare the results to those of a more suitable estimation procedure. Thus, illness duration was also investigated using Poisson regression, and the comparison between Poisson and OLS is discussed below.

#### Some Problems of Estimation

A pervasive problem in the estimation of the effects of air pollution on illness is that information on personal exposure to pollutants is rarely available. Researchers have been obliged to use ambient monitoring data as a proxy for personal exposure, and our study is no exception to this rule. Nonetheless, every child in our sample lived and attended school within a mile of a monitoring site, a relatively tight radius compared to most similar studies.

Besides this measurement difficulty, there were several major econometric problems. These problems arose primarily from our desire to use a linear probability model and OLS as the principal estimation procedure. Convenient though it may be, the OLS model requires a number of assumptions of questionable validity for the current problem. The question we now examine is whether these refinements make much difference to outcomes.

The first problem is that the dependent variable  $S_{ijt}$  is limited to the values 0 or 1 (for illness incidence) or to the small positive integers (for illness duration). Thus, the OLS estimators are not efficient, and the linear probability model may not be appropriate in any event.

A second problem is concerned with the functional form of the relationship between illness and air pollution (indeed, between illness and any explanatory variable). As there is no theory to guide the selection of functional form, we chose a functional form on the basis of an information criterion proposed by Sawa.<sup>21</sup>

The third problem involves the structure of the disturbance term  $\epsilon_{ijt}$ . We examined two alternatives to the OLS assumption of uncorrelated disturbances:

**Autoregression:** an individual's health status in one period may affect his or her health status in subsequent periods, in which case  $E(\epsilon_{ijt}\epsilon_{ijt'}) \neq 0$  for  $t \neq t'$ .

**Contagion:** one's health may be affected by the health of others, especially family members and classmates, in which case  $E(\epsilon_{ijt}\epsilon_{ijt'}) \neq 0$  for  $i \neq i'$  or  $j \neq j'$ .

These problems were examined sequentially. First, several alternative functional forms were examined. Having selected a functional form, we then examined the error structure. Finally, alternative estimation procedures more suited to limited dependent variables were investigated.

#### Functional Form

Table IV shows the relationship between illness incidence and NO<sub>2</sub> for several different specifications of the pollution variable. The basic variable was NO2MAX, the daily maximum NO<sub>2</sub> reading, averaged over the two-week period. (Not shown are specifications using average pollution variables, which give results inferior to the ones for NO2MAX.)

The specifications examined include the following:

- linear specification
- quadratic
- cubic
- piecewise linear functions with one break point at 100  $\mu\text{g}/\text{m}^3$ , two break points at 75 and 150  $\mu\text{g}/\text{m}^3$ , and three break points at 75, 100 and 150  $\mu\text{g}/\text{m}^3$ .

In all specifications, except the linear, the relationship between NO<sub>2</sub> and illness incidence is U-shaped. Based on



Table VI. Comparison of logit and OLS models predicting illness incidence.

	OLS		Logit		$\frac{\partial S}{\partial x}$
	Coefficient	Std. error	Coefficient	Std. error	
Intercept	0.176	0.029 <sup>a</sup>	-1.80	0.256	
NO2MAXL	-8.98E-4	2.04E-4 <sup>b</sup>	-0.0067	0.00174 <sup>b</sup>	-7.63E-4 <sup>b</sup>
NO2MAXH	1.61E-4	0.68E-4 <sup>a</sup>	0.00135	0.000595 <sup>a</sup>	1.53E-4 <sup>a</sup>
PAR90P	-2.63E-4	0.923E-4 <sup>a</sup>	-0.00187	0.00082 <sup>b</sup>	-2.13E-4 <sup>a</sup>
SUL90P	2.55E-4	12.1E-4	-0.00138	0.0108	-1.57E-4
AGE	-0.0082	0.00085 <sup>b</sup>	-0.0715	0.0074 <sup>b</sup>	-0.00814 <sup>b</sup>
CROWD	0.150	0.0071 <sup>a</sup>	0.151	0.064 <sup>a</sup>	0.0172 <sup>a</sup>
EPIDEM	0.074	0.010 <sup>b</sup>	0.537	0.087 <sup>a</sup>	0.061 <sup>b</sup>
GAS	-0.020	0.012	-0.187	0.110	-0.020
RAIN	-0.0063	0.0016 <sup>b</sup>	-0.061	0.015 <sup>b</sup>	-0.0058 <sup>b</sup>
TEMP	0.00184	0.00039 <sup>b</sup>	0.0167	0.00356 <sup>b</sup>	0.00190 <sup>b</sup>
RACE1W	0.0540	0.0088 <sup>b</sup>	0.542	0.093 <sup>b</sup>	0.0528 <sup>b</sup>
CHRON	0.0418	0.0059 <sup>b</sup>	0.350	0.0450 <sup>b</sup>	0.0423 <sup>b</sup>
CHESTINF	0.0460	0.0102 <sup>b</sup>	0.342	0.081 <sup>b</sup>	0.0434 <sup>b</sup>

<sup>a</sup> Significant at the 5% level.<sup>b</sup> Significant at the 1% level.

the BIC criterion proposed by Sawa,<sup>21</sup> the best performer is the piecewise linear specification with a break point at 100  $\mu\text{g}/\text{m}^3$ .

We also tested these spline specifications against the quadratic specification using one of the tests described by Davidson and MacKinnon<sup>22</sup> for non-nested models. The result of this test was as follows: When the quadratic specification was taken as the null hypothesis against the piecewise linear alternative, the null hypothesis was rejected. However, with the spline taken as the null hypothesis the null could not be rejected. Thus, the spline specification with a break point at 100  $\mu\text{g}/\text{m}^3$  fit the data best, and this was used in subsequent work.

#### Error Structure

To examine the effect of possible serial correlation we assumed a first-order autocorrelation scheme and used a two-stage procedure described by Kmenta.<sup>23</sup> First we estimated the autocorrelation parameter  $\rho$  using OLS, and then reestimated the model

$$(Y_i - \hat{\rho} Y_{i-1}) = (X_i - \hat{\rho} X_{i-1})\beta + (\epsilon_i - \hat{\rho} \epsilon_{i-1}).$$

Our estimate for  $\rho$  was  $\hat{\rho} = 0.036$ . In the second stage, we found the following results for the NO<sub>2</sub> variables, which, it will be noted, are essentially the same as Column H of Table III:

$$S = -9.35\text{E-}4 \text{ NO2MAXL} \\ (2.12\text{E-}4) + 1.76\text{E-}4 \text{ NO2MAXH} + \text{other terms} \\ (0.81\text{E-}4)$$

with  $n = 14907$  and  $F = 25.1$  for the equation. This result indicated that the problem of autocorrelation could be ignored.

Contagion presented a problem that we were not able to resolve fully, due to a lack of complete information on all the physical contacts among the various members of the sample. However, we were able to examine contagion in the home, one of the most likely places where diseases may be spread.

If contagion in the home is present, the estimated effect on incidence and duration of variables common to members of a family, such as their exposure to air pollutants, will exceed the true effect. To test for this possibility we compared regression results from the full sample to the results from a subset consisting of one child chosen randomly from each family represented in the sample (Table V). Although the standard errors on the former are a bit larger, (which is what one would expect from the reduction in sample size), the coefficients are quite similar. Thus, the results are probably not much affected by spread of disease in the home.

#### Limited Dependent Variables

In this section we examine whether the results depend on our use of OLS rather than techniques more suited to limited dependent variables. Specifically, we tested the linear probability model against a logit model for predicting illness incidence, using the "C" test described by Davidson and MacKinnon.<sup>22</sup> This test showed the logit model to be superior in the following sense: When the null hypothesis  $H_0$  is the

Table VII. Comparison of Poisson and OLS models predicting illness duration.

	OLS		Poisson		$\frac{\partial S}{\partial x}$
	Coefficient	Std. error	Coefficient	Std. error	
Intercept	0.352	0.079 <sup>b</sup>	-1.62	0.361 <sup>b</sup>	
NO2MAXL	-0.00249	0.00056 <sup>b</sup>	-0.0083	0.0023 <sup>b</sup>	-0.00173 <sup>b</sup>
NO2MAXH	0.00043	0.000186 <sup>b</sup>	0.00195	0.00084 <sup>a</sup>	0.00041 <sup>a</sup>
PAR90P	-0.0047	0.00025	-0.00101	0.00120	-0.0021
SUL90P	-0.0026	0.0033	-0.0120	0.016	-0.0025
AGE	-0.0174	0.0023 <sup>b</sup>	-0.078	0.0102 <sup>b</sup>	-0.0162 <sup>b</sup>
CROWD	0.0089	0.0193	0.075	0.092	0.0156
EPIDEM	0.216	0.028 <sup>b</sup>	0.768	0.117 <sup>b</sup>	0.160 <sup>b</sup>
GAS	-0.032	0.031	-0.155	0.158	-0.030
RAIN	-0.0044	0.0042	0.0022	0.0195	0.00046
TEMP	0.0030	0.0011 <sup>b</sup>	0.0152	0.0052 <sup>b</sup>	0.0032 <sup>b</sup>
RACE1W	0.119	0.024 <sup>b</sup>	0.688	0.148 <sup>b</sup>	0.114 <sup>b</sup>
CHRON	0.091	0.016 <sup>b</sup>	0.399	0.069 <sup>b</sup>	0.093 <sup>b</sup>
CHESTINF	0.178	0.028 <sup>b</sup>	0.571	0.097 <sup>b</sup>	0.155 <sup>b</sup>

<sup>a</sup> Significant at the 5% level.<sup>b</sup> Significant at the 1% level.

OLS model and the logit model is  $H_1$ .  $H_0$  is rejected; however, when the roles are reversed and  $H_0$  is the logit model,  $H_0$  cannot be rejected.

For illness duration a similar comparison was made between OLS and Poisson regression. Again, the OLS model was found to be inferior. Nonetheless, the coefficients on the independent variables estimated using OLS were very similar to the corresponding coefficients for the logit and Poisson models. These coefficients are compared in Tables VI and VII. To facilitate comparison, the rightmost column of each table is the derivative of the dependent variable of the Poisson or logit function, evaluated at the mean of the dependent variable. (For discrete independent variables the entry is the average change in probability of illness, estimated by the weighted sum of the change in probability when the variable is added at the mean and when it is taken away.) Even though OLS appeared slightly inferior to logit and Poisson regression in predicting illness incidence and duration, the qualitative results were hardly affected.

### Conclusions

A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between  $\text{NO}_2$  ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and  $\text{NO}_2$  concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. As far as we know, there is no clinical explanation for this result. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

The strange relationship between  $\text{NO}_2$  concentrations and ARD in children could be attributable to three problems inherent in any epidemiological study. First, the relationship could be entirely fortuitous, although the odds against this for our study are long. Second, both illness and  $\text{NO}_2$  could be related to some unobserved variable. However, such a variable must have strange properties, because for certain well-defined subsets, its relationship to either illness or  $\text{NO}_2$  changes substantially. Finally, the data could still contain biases that create the observed effects.

In short, there is reason to be skeptical of a U-shaped dose-response function relating ambient  $\text{NO}_2$  levels and acute respiratory disease. Nonetheless, we suggest that non-monotonic dose-response functions be explicitly considered in future epidemiological or clinical research on the health effects of  $\text{NO}_2$  and perhaps other pollutants as well.

### Acknowledgments

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14

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Watkins, C.J., Sittampalam, Y., Morrell, D.C., Leeder, S.R., Tritton, E. "Patterns of respiratory illness in the first year of life" British Medical Journal 293:794-796, 1986.

ABSTRACT: This paper describes a study of respiratory illness during the first year of life in a cohort of infants who were born between 1975 and 1978 to mothers who were registered with two inner London group general practices. The types of respiratory illness and their relation to the season of the year and season of birth of the child are examined. The relations among the frequency and type of respiratory illness and several social and family factors that have previously been shown to be associated with high levels of respiratory morbidity are also described.

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Details of self help groups are included in the newsletter. Usually between four and six groups function in the practice at one time.

These have included relaxation, yoga for men, first time mothers, parents of teenagers, and groups for those who wish to lose weight or give up smoking. The newsletter also contains items of health information—for instance, on hypothermia, flu risk, taking your temperature, food labelling, and maintenance for holidays. Other items have included items of road dangers, book reviews, articles on the history of the practice, details of fundraising events held by the Practice Participation Association, and local issues related to health.

The newsletter covers four sides of A4 paper. A typical front page is shown in the figure.

#### How is the newsletter distributed?

During 1982 the practice register was arranged geographically by volunteers to create a street index. It is thus possible to identify patients who live in a household, and labels are printed with the names of individual patients, one label per household. The task of reorganising the practice register of 11,500 patients geographically would probably occupy a full time person for about three weeks.

Two voluntary managers organise the distribution of newsletters to individual households. One hundred and twenty volunteers have been recruited by advertisement in the newsletter and in the surgery. Most deliver 50 to 100 newsletters in a geographically limited area, usually near their homes. To meet the requirements of the local medical community that the newsletter should not be construed as advertising for the practice, each newsletter is folded in three, leaving the outside largely blank, and sealed with an address label.

The cost of producing each edition of the newsletter is approximately £150. This is met by the association, which has a successful fundraising group. The cost is low only because of the enormous amount of voluntary help offered by members of the practice. The self adhesive address labels cost £45 to produce for each edition, and

BRITISH MEDICAL JOURNAL VOLUME 293 27 SEPTEMBER 1986  
this is met by the practice—the only cost to the doctors of the newsletter.

#### What does the newsletter achieve?

To assess what impact the newsletter has on members of the practice, a survey was carried out of patients' views of the newsletter. 178 patients who attended one of the surgeries and 42 patients who attended an open meeting of the association completed a questionnaire. Of these patients, 76% had heard of *Building Well*, most of whom knew that it was the newsletter of the practice association; 65% had read the last issue, though only 42% could remember a specific item in the last issue. Few patients made negative comments about the newsletter in the questionnaire, and no one has ever asked to be excluded from its delivery list.

There have been few spontaneous contributions from patients, but many people tell the deliverers that they welcome the newsletter, and several new patients have said how impressed they were by the evidence of community feeling in the practice. Delivering the newsletter is a simple task, and many people seem to enjoy having the opportunity to give something back to the practice in this way. Several have become group leaders or fundraisers, and the newsletter clearly performs an important recruiting role for the Practice Participation Association.

#### Conclusion

The practice newsletter has been produced regularly for three years with voluntary help, and thus the cost can be supported by the Practice Participation Association. Delivering it to households provides an unusual way of informing all members of the practice of the association's activities. It is hoped that the newsletter helps to promote a feeling among patients that they belong to a practice "community."

(Received 18 July 1986)

## Practice Research

### Patterns of respiratory illness in the first year of life

C J WATKINS, Y SITTAMPALAM, D C MORELL, S R LEEDER, E TRITTON

#### Abstract

This paper describes a study of respiratory illness during the first year of life in a cohort of infants who were born between 1975 and 1978 to mothers who were registered with two inner London group general practices. The types of respiratory illness and their relation to the seasons of the year and seasons of birth of the child are examined. The relations among the frequency and type of

respiratory illness and several social and family factors that have previously been shown to be associated with high levels of respiratory morbidity are also described.

#### Introduction

An association between various personal and family factors and an increased respiratory morbidity in children has been identified.<sup>1-3</sup> These community surveys have relied on the mothers' responses to questionnaires at interview about their infants' health to estimate the occurrence of respiratory illness. Such estimates have disagreed substantially with estimates derived from direct studies of respiratory illness in patients who have presented to attending general practitioners.<sup>4-6</sup>

Most serious respiratory illness in infancy is managed by general practitioners. Apart from the need for accurate diagnosis and effective treatment for the acute illness, the problem for the attending general practitioner is to identify and treat appropriately

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41.4-50.1) and 33.9/100 children (9% confidence limits 24.6-47.5) of parents in non-manual occupations.

The effect of the parents' occupation might have represented a difference in the propensity of the mother to consult for her and child. Examining the frequency of consultation for non-respiratory illness by parents' occupation did not confirm this, suggesting that the high frequency of consultation for lower respiratory illness in children of those in manual occupations was due to a higher frequency of episodes of lower respiratory illness rather than a behavioural difference of the social classes.

TABLE 1—Exposure of respiratory illness recorded by the general practitioner in a birth cohort of 464 children

Exposure of respiratory illness	No./% of children
No respiratory illness	78 (16.8)
Upper respiratory illness only	171 (36.9)
Lower respiratory illness	169 (36.4)
Other respiratory illness	88 (19.0)
The episode	21 (4.5)
Two episodes	11 (2.3)
Three or more episodes	10 (2.2)
Upper and lower respiratory illness	111 (23.9)
All upper respiratory illness	79 (17.0)

TABLE 2—Relation between parental social and family factors and the annual rate of lower respiratory illness per 100 children per year presented in a birth cohort of 464 children

Sex	No.	Annual rate per 100 children	95% confidence interval	Significance level
Boy	204	34.4	40.5-31.3	$p < 0.05$
Girl	260	34.3	41.3-26.1	
Parent's occupation*				
Non-manual	160	37.3	29.1-46.3	$p < 0.01$
Manual	224	29.4	33.5-25.7	
Marital status with child				
Yes	179	42.9	34.5-51.7	$p < 0.01$
No	225	46.3	51.3-40.1	
Parent smoking†				
Smoker	137	46.2	38.4-54.1	
Non-smoker	80	23.0	21.5-24.6	$p < 0.01$
Parent only	35	34.9	31.3-38.5	
Non-parent only	118	37.6	43.0-32.2	
Parent occupation*				
Smoker	240	34.2	41.4-26.2	
Non-smoker	40	48.1	51.3-40.1	
Parent only	35	34.9	31.3-38.5	
Non-parent only	31	61.3	42.4-79.6	$p < 0.1$

\* Excludes 15 children in whom no information about father's occupation, mother's occupation, or respiratory symptoms was available.

## Discussion

Because of the wide interdoctor variation in the diagnosis of respiratory illness we have avoided using terms such as bronchitis, pneumonia, bronchiolitis, and wheezy bronchitis. For similar reasons we have avoided using "whooping" or "croup-like," for example, in describing lung sounds but instead have described the consultations for illness according to whether or not asthmatic sounds were heard in the lung fields and defined episodes of respiratory illness accordingly.

The high peak of respiratory illness in the winter months, and in particular the peak of incidence of lower respiratory illness occurring in the month of February, strongly suggest infection. In addition, the relation of season of birth to respiratory illness further supports infection as a major factor. The lower frequency of both upper and lower respiratory illness occurred in the first three months of life. The peak for both is in the winter months for children who were born in the spring, summer, and autumn. For those born in winter few upper or lower respiratory illnesses were recorded in their first winter. In the second winter the expected seasonal peak of upper respiratory illness occurred, but a lower rise of lower respiratory illness was noted. Inherited maternal immunity presumably protects these children during the winter months

immediately after birth. By the time they are exposed in the second winter their defence mechanisms have matured sufficiently to protect them from infection. The role of immunity can be clarified only when simple methods of identifying viruses and of measuring the immune status of children become available for use in general practice. Studies carried out in hospital are unlikely to be helpful—only those of the 464 children in our study were admitted to hospital.

In this study the role of family health and social variables is not as clear cut as that reported by Leader *et al.*<sup>1</sup> The striking finding in this study is the social class difference in frequency of consultation for respiratory illness, with high consultation rates for those whose fathers were in manual occupations. This is not explained by the fact that the families from which such children arose are more likely to live in overcrowded conditions nor that the parents are more likely to smoke and have a productive cough nor that mothers of such children were less likely to breast feed. The fact that the propensity to consult for non-respiratory illness was similar for children whose fathers were in manual and non-manual work indicates that this is not a behavioural characteristic but is a true representation of the differential frequency of occurrence of respiratory illness according to parental occupation.

Several conclusions arise from this study. Episodes of lower respiratory illness, defined as those in which there were one or more consultations at which asthmatic lung sounds were recorded, are particularly frequent in the children of manual workers. This cannot be explained by the many social and family variables examined in this study such as overcrowding, smoking habits, parents' respiratory symptoms, and breast feeding. The relative freedom from respiratory illness in the first three months of life and the seasonal incidence of lower respiratory illness in children who were born in the winter reinforces the inference (as opposed to allergic aetiology of lower respiratory illness in young children. Further studies of the aetiology of respiratory illness in children may more usefully focus on nutrition and immunity than on the traditional methods of environmental pollution.

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SUMMARY: The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking) on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year; a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.6% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

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# A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario

## Epidemiologic Survey Design, Methods, and Description of Cohort<sup>1-3</sup>

ANTHONY T. KERIGAN, CHARLES H. GOLDSMITH, and L. DAVID PENGELLY

### Introduction

The study of environmental factors responsible for respiratory disease in children is important for 2 reasons: (1) the absence of confounding factors, such as personal smoking and occupation, makes the interpretation of any observed association between air quality and respiratory disease more credible; and (2) the growing realization that respiratory illness during childhood may predispose to the development of respiratory morbidity and early mortality from respiratory illness during adult life (1, 2).

This particular usefulness of children has become more important as air quality has improved during the last decade (1970-1979) and levels become closer to the Ontario guidelines. For total suspended particulates (TSP), the Ontario objective (annual geometric mean) is 60  $\mu\text{g}/\text{m}^3$ . In 1978, the annual TSP in Hamilton was 77  $\mu\text{g}/\text{m}^3$ . For sulphur dioxide, the objective is 0.02 ppm annual average and the measured level was 0.016 ppm (3).

Studies in several countries from 1967 to 1978 have identified a number of environmental factors that might lead to respiratory disease in children. The initial study of the effect of the particulate/sulphur dioxide ( $\text{SO}_2$ ) complex was conducted by Lunn and coworkers (4) and showed increased prevalence of respiratory symptoms and reduced pulmonary function in areas of poor air quality. Improvement in air quality led to a reduction in these adverse health effects (5). Follow-up studies in several towns in the United Kingdom by Melia and colleagues (6) showed that adverse health effects were now extremely difficult to find with the further improvement in air quality. These studies, however, did not consider the possible role of parental smoking.

As outdoor air quality improved, at-

**SUMMARY** The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking), on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year, a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.8% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

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tention changed to indoor air quality, particularly in relation to parental smoking and indoor sources of gaseous pollutants such as gas stoves. The health effects from parental smoking appear to be most marked in the first years of life (7), but studies of this effect on older children have not yielded consistent results, some showing increased prevalence of symptoms (8) but others showing no effect (9, 10). Colley and coworkers (11) suggested that the effect of parental smoking may be due predominantly to the increased prevalence of parental cough. An effect of parental smoking on children's pulmonary function has also been shown (12, 13). The influence of gas cooking was first suggested by Melia and coworkers (14), although the effect seemed to decrease as the children became older. In contrast, Keller and colleagues (15) were not able to find any effect of gas cooking on children's respiratory symptoms.

The uncertainty about the role of low levels of TSP and  $\text{SO}_2$ , and their importance in relation to domestic environmental factors, led us in 1978 to initiate a 3-

yr cohort study in Hamilton, Ontario that was designed to answer the following questions. (1) Is there an effect on children's respiratory health of suspended particulates and  $\text{SO}_2$  at the present levels? (2) What is the effect of the various factors in the domestic environment when considered in relation to outdoor air quality?

The main study was preceded by a pi-

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TABLE 1  
SUSPENDED PARTICULATE LEVELS BY AREA OF CITY  
(JANUARY THROUGH DECEMBER 1980)

	WU	EU	WL	EL	IC
Total suspended particulates, $\mu\text{g}/\text{m}^3$ *	44	43	61	58	90
TSP Load < $7.0 \mu$ , %	70.3	66.8	67.9	71.1	62.1
Maximal daily average, $\mu\text{g}/\text{m}^3$ †	140	146	173	149	223
Monitoring sites, n	5	3	9	4	5

Definition of abbreviations: WU = west upper quadrant; EU = east upper quadrant; WL = west lower quadrant; EL = east lower quadrant; IC = industrial core.

\* Average of annual geometric means of all sites in each area.

† Average of daily maxima of all sites in each area.

lot study (16) which demonstrated that within Hamilton, Ontario, there existed substantial gradients across the city for suspended particulates and  $\text{SO}_2$  that would enable us to study children with differing exposures in the same city. This offered major logistical advantages in a design similar to that of Lunn and co-workers (4). During the current study, these gradients for suspended particulates continued to be present. The levels in each area of the city during 1980 are shown in table 1 in terms both of the annual geometric mean and of the daily maximum. The table also shows the proportion of particulate load less than  $7.0 \mu$ . Despite the increasing level of particulates towards the industrial core, there is little change in the proportion of particulate matter less than  $7.0 \mu$ .

## Methods

### Design of Study

Hamilton, with a population of approximately 300,000, is a city situated at the western end of Lake Ontario. The dominant geographic feature is an escarpment of approximately 100 m high that runs from east to west, effectively dividing the city into a lower section and a mountain section. The city is industrial, with the heavy industrial core, located in the northeast section of the city, being the dominant producer of particulate and  $\text{SO}_2$  emissions, although there is a secondary  $\text{SO}_2$  area source in the commercial section located in the western part of the city. Prevailing winds are from the southwest.

Initial air quality monitoring during the pilot study had indicated the presence of substantial gradients for both particulates and  $\text{SO}_2$ , with the mountain section having lower levels than the lower section of the city. On this basis and on the knowledge of prevailing winds, we divided the city into 4 quadrants (figure 1) for the purpose of selection of the sample to be studied. The sampling frame was all public elementary schools within the city of Hamilton. Sample size considerations dictated that at least 800 children would be required within each quadrant. A difference of 5 to 7% in the mean of a particular pulmonary function variable was felt to be neces-

sary for biologic significance. One of the principal outcomes of interest was the measurement of air flow, especially at low lung volumes. Estimates of the mean and standard deviation of these variables were obtained from our pilot study (16) ( $\text{FEV}_{0.1}$ : mean, 1.79 L; SD, 0.36;  $\text{MEF}_{0.1}$ : mean, 1.09 L/s; SD, 0.44). The first criterion employed in sample size determination was that there should be only a 10% chance of missing a biologic difference (Beta error = 0.1). A second criterion was that a difference was considered to exist between the 2 samples if the appropriate statistical test showed that the observed difference had only a 5% chance of occurring in the absence of any real difference (Alpha error = 0.05). Within each of these quadrants, schools were randomly selected until at least 800 children from Grades 2, 3, and 4 during the initial school year had been included. The only children excluded were those older than 10 yr of age by the end of 1978. All children in the required grades from the final school selected in each quadrant were chosen. The children included in the first year of testing made up the initial cohort.

After more detailed air quality monitoring during the first year of the study, it was realized that the area of highest exposure (i.e., TSP annual geometric mean  $> 60 \mu\text{g}/\text{m}^3$ ) was underrepresented, despite the initial stratification by quadrants in the original design. For this reason, the 3 remaining schools in this area were added, with all children within the required age interval being included.

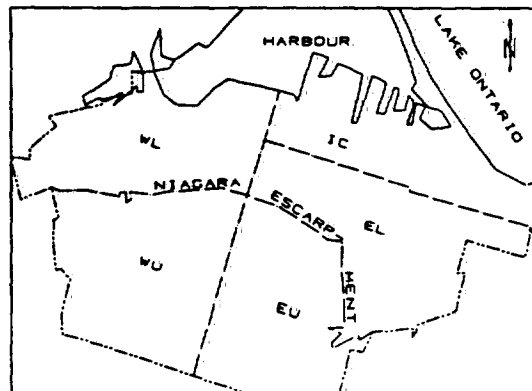
In addition, in the second year, all children

in this same age interval as the initial cohort who moved into a school of study were included in the study. During the third year, no new children were added.

The questionnaire used in the study was one that we had employed in the pilot study. It was developed from a questionnaire used in a similar study in the European Economic Community. The questionnaire covered several aspects of the child's respiratory history, family smoking and respiratory profile, certain aspects of the child's medical background, and information relating to the quality of the dwelling and socioeconomic circumstances of the family. There were differences between our questionnaire and that developed by the American Thoracic Society (17). In our questionnaire, a distinction was made between morning cough and cough during the day or night, the respondent being asked if the child usually coughed in the morning or during the day or night, respectively. Sputum production was not asked about. The question on wheezing inquired if the chest ever sounded wheezy or whistling. In addition, a question about asthmatic attacks in the previous 12 months was included. Two questions related to acute respiratory illness were included. The first asked about a period of cough and phlegm lasting for 3 wk or more and the second about any chest illness keeping the child home for a week or more. (A detailed questionnaire is available from the writers.) In Year 2, questions about early childhood illnesses were added that were derived from the questionnaire designed by the American Thoracic Society (17). Our questionnaire was administered in the home by a trained interviewer to the mother or female guardian, or in her absence, to the father or male guardian. The questionnaire was administered in each of the 3 yr of the study prior to the performance of pulmonary function testing.

Pulmonary function testing was performed at the child's school. Four types of pulmonary function tests were performed: forced expired maneuvers ( $\text{FEV}_{0.1}$ , FVC,  $\text{MEF}_{0.1}$ ,  $\text{MEF}_{0.25}$ , and MET), spirometry (a slow vital capacity (VC) following quiet breathing) (VC, ERV), single-breath nitrogen washout (CV/VC,  $\text{N}_2$  difference) and multiple-breath

Fig. 1. Outline map of Hamilton, Ontario, showing the 4 quadrants chosen in the original design, and the Industrial Core (IC) (WU = west upper; EU = east upper; WL = west lower; EL = east lower).



nitrogen washout (FRC). The additional use of the single-breath nitrogen washout was justified by the study of Becklake and coworkers (18), who showed an increase in closing volume in children exposed to a high particulate/SO<sub>2</sub> environment.

Air quality was measured by a comprehensive particulate and SO<sub>2</sub> network. There were 27 monitored sites for TSP using hi-vol samplers, with 9 additional hi-vol samplers with Andersen 4-stage cascade impactors for the measurement of mass median diameter. In addition, there were 16 sites for SO<sub>2</sub> monitored in groups of 8, using Beckman 906A monitors (Beckman Instruments, Fullerton, CA), for 6-wk periods in rotation. These sites were distributed throughout the city. Details of air quality monitoring will be contained in a subsequent report.

#### Protocol

In the questionnaire survey, interviewers were randomly assigned to eligible children at each school to be visited, thus ensuring that several interviewers would be assigned to each school. In addition, interviewers were rotated to schools in different parts of the city. The parents had been informed in advance by letter to expect a phone call from the interviewer. The letter also described the purpose of the study as being the investigation of the child's respiratory health. No mention was made of air pollution. Each interviewer telephoned the parent or guardian to arrange for an appointment for questionnaire administration. There was provision for 3 call-backs, if no contact was established initially, before no further attempt at interviewing was made. At the time of contact, the interviewer was able to screen out those children who were older than 10 yr of age in the first year of testing. If the parent consented to the interview, they were then visited by the interviewer. The percentage of those eligible, for whom an interview was not obtained, including those with whom no contact could be established, ranged from 4.6% in Year 1 to 3.3% in Year 3 (table 2). No further attempt was made to follow these. Interpreters were used as necessary, but were required for less than 1% of the parents. At the end of the interview, the pulmonary function test was explained to the parent or guardian, and written consent for the test was obtained at that time. The completed questionnaire was then returned for coding, keypunching, and data storage at the Computation Services Unit at the Health Sciences Centre, McMaster University.

Pulmonary function testing was performed, throughout the school year, within 4 wk of the completion of the interview. Two teams of pulmonary function technicians were assigned alternately to a school in the upper and in the lower part of the city. The testing routine was explained initially to all the students at an assembly and explained further to each child at the time of his or her testing. A questionnaire about smoking habits was also administered to the child at the time of testing in the third year of the study. Pulmo-

TABLE 2  
CONSENT AND TESTING RATE FOR SAMPLE

	Year 1	Year 2	Year 3
Eligible for interview	3,505	3,727	3,168
Interviews completed	3,345	3,588	3,065
Interview completion rate, %	95.4	96.3	96.7
Consents given for testing	3,329	3,573	3,055
Consent rate, %	95.0	95.9	96.4
Number tested	3,131	3,439	2,949
Testing completion rate, %	89.3	92.3	93.1

nary function testing was performed using the Hewlett-Packard 47804A Pulmonary Calculator System (Hewlett-Packard, Waltham, MA). In this system, flow is measured by a pneumotachygraph, and volume is computed internally by integration with time. Calibration of the 2 systems used was performed twice daily with a 2-L syringe. Correction for ambient temperature and pressure was performed internally by the computer system by entering the appropriate values. After measurement of height and weight, the child first performed a multiple-breath nitrogen washout. This was followed by at least 3 forced expired maneuvers. For acceptance, the 2 largest FVC values had to be within 5% of each other. All measurements were taken from the maneuver with the greatest sum of FVC and FEV<sub>1</sub>. Spirometry was then performed. If the VC obtained was less than the FVC by more than 10%, the spirometry was repeated until the estimate was within 10%. However, if the VC was greater than the FVC by more than 10%, then the forced expired maneuver was repeated until the FVC estimate was within 10% of VC. Finally, at least 2 single-breath nitrogen washouts were performed in which the expired nitrogen concentration was continuously plotted against VC. The method used was that of Mansell and associates (19), but without the additional dead space. For acceptance of the single-breath nitrogen washout test, the VC had to be within 10% of the largest previous VC from spirometry. If both single-breath maneuvers were acceptable, then the closing volume from the maneuver with the greater VC was taken for analysis. The presence of an upper or lower respiratory infection was noted by the technician at the time of the test. However, the test was always performed, the infection data to be used at the time of analysis to estimate the effect of the infection on pulmonary function. The testing followed the same sequence in Years 2 and 3, except that in Year 3, the single-breath nitrogen washout was omitted because of poor reproducibility (see DISCUSSION). The child was not necessarily tested with the same system nor by the same technician, but comparison of results from the 2 teams was performed at regular intervals to identify any systematic differences.

All measurements of flow and of volume were computed internally, with output being recorded by an on-line printer. Closing volume, however, was computed by inspection

of the single-breath nitrogen washout curve, and was taken at that point of inflection of the nitrogen washout curve from a line drawn through phase 3 of the curve (19). These results were then returned for coding, keypunching, and data storage in a manner similar to the questionnaire data.

The quality control of the data gathered was performed in several ways. For both the questionnaire and the pulmonary function coding, a random 5% sample of the data was recoded by a second coder. The reliability of the questionnaire data was estimated by the random selection of 4 interviewers after each pair of schools was completed. For each interviewer, 2 interviews were randomly chosen, and within those interviews, 2 questions were randomly selected. The appropriate respondent was then phoned and the questions were asked again. Apart from estimating the reliability of the answers, this procedure also verified that the original interview had indeed taken place. Interinterviewer variation or bias was estimated by comparing the response rates to certain questions obtained by each interviewer. These data were then examined to see if any differences between interviewers might be greater than that caused by chance alone. When such a difference was found, interviewing technique was reviewed to ensure consistency of technique. In no case was it necessary to change any of the interviewing staff because of poor reliability.

The reliability of the pulmonary function testing was estimated by the retesting of 8 children in each school, 2 children randomly chosen from each age group. All data from pulmonary function testing were passed through a range checking program after data storage, the range being 4 standard deviations centered at the mean, these interval estimates of parameters being derived from the original pilot study. Finally, we were interested in determining any systematic differences between the 2 pulmonary function testing teams. The presence of any differences was estimated by parallel line regression analysis for 4 of the variables measured (FVC, MEF<sub>25</sub>, MET, and CV/VC). This technique used regression analysis to fit a regression line separately to the data collected by each team; if the linear relationship was the appropriate model, then the hypothesis that the 2 lines were parallel was tested. If this hypothesis was not rejected, then the hypothesis that the intercepts were the same was tested. If the second hypothesis was

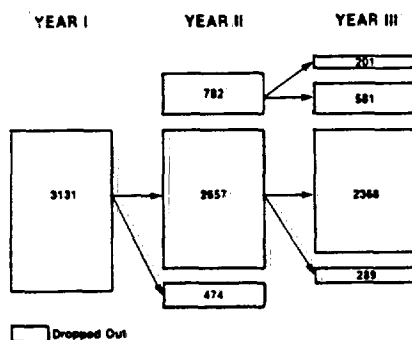


Fig. 2. Maintenance of cohort size, showing numbers lost by attrition and Industrial Core group added during Year 2.

not rejected then it was concluded that the regression lines for the 2 teams were coincident (20).

A final quality control measure was an examination of the proportion of missing values for each variable for each team, as an indicator of systematic differences between the 2 teams. The analysis and the results of these quality control measures will be described in detail in a separate report. However, the reliability of the questionnaire and pulmonary function data, and the success rates of pulmonary function testing, are described in this report.

Statistical analyses were performed by subprograms in the Statistical Package for the Social Sciences (21). The difference between sample means was tested for significance by subprogram *t* test for paired samples. Pearson's product-moment correlation coefficient, as a measure of association of 2 independent variables, was computed by subprogram scattergram. Hypothesis tests were all two-tailed.

## Results

### Characteristics of Cohort

The number who were eligible for testing in each year of the study is shown in table 2. To be eligible, the child could

not have attained his or her eleventh birthday before December 31, 1978. This table also shows the interview completion rate obtained in each year. The rate, which was above 95% for each year, is considered acceptable. In addition, the percentage giving consent for the pulmonary function testing was virtually identical to that giving consent for interview. There was, however, a degree of attrition after consent was given for pulmonary function testing, before the test was performed. The major reason for this was the child having moved from a testing school into a nontesting school during the time between consent and testing. This attrition was less in Years 2 and 3.

An important feature of the study was

the ability to follow the initial cohort into the second and third years of the study. The particular importance of this is the ability to measure changes in pulmonary function variables as the child grows. It is possible that the rate of change of a particular pulmonary function variable might be a more sensitive outcome measure than the use of a single point estimate. The number of children with pulmonary function testing in Year 1 who were tested in Years 2 and 3 (approximately 75% of the original cohort) is shown in figure 2. The figure also shows the number of children added in Year 2 and how many of these were followed into Year 3. The characteristics of the children at the time of pulmonary function

TABLE 3  
CHARACTERISTICS OF SAMPLE TESTED

	Year 1		Year 2		Year 3	
	(n)	(%)	(n)	(%)	(n)	(%)
Male	1,611	51.5	1,789	51.4	1,513	51.3
Female	1,520		1,670		1,436	
Caucasian	2,876	91.9	3,161	91.9	2,723	92.3
Non-Caucasian	255		278		226	
Total	3,131		3,439		2,949	

TABLE 4  
PREVALENCE OF DOMESTIC FACTORS BY AREA OF CITY: YEAR 2\*

	WU	EU	WL	EL	IC
Number	629	878	741	863	242
Mother smoke	37.3	42.5	42.2	48.2	60.1
Father smoke	38.3	43.4	43.3	50.2	61.3
Mother cough	15.7	15.0	17.8	17.5	28.5
Father cough	22.1	26.4	26.1	25.6	40.4
Gas cooking	8.3	8.3	29.7	15.6	43.4
Share room with 2 or more	2.3	3.6	7.3	7.0	8.8
Income less than \$10k/yr	15.8	11.3	20.7	15.6	25.9
Less than 2 yr at present address	22.4	19.0	28.2	25.6	34.4

For definition of abbreviations, see table 1.

\* Values are percentages. Data missing on 35 subjects.

TABLE 5  
PREVALENCE OF SMOKING\*

	Age (yr)						Total
	8	9	10	11	12	13	
Any history of smoking†							
Yes	0 (0)	57 (11.8)	175 (18.1)	250 (28.3)	188 (37.8)	37 (50.0)	707 (24.3)
No	3	425	791	634	310	37	2,200
Total	3	482	966	884	498	74	2,907
Smoking in last 4 wk‡							
Yes		2 (3.6)	28 (16.4)	41 (17.0)	56 (30.8)	12 (32.4)	139 (20.3)
No		53	143	200	126	25	547
Total		55	171	241	182	37	686

\* Values are frequency with percentages in parentheses.

† Missing observations, 158.

‡ Missing observations, 21.

TABLE 6  
REPEATABILITY OF RESPIRATORY SYMPTOM QUESTIONS

Question	Raw Agreement	Chance-Corrected Agreement (Kappa)
Cough in morning	0.92	0*
Cough during day or night	0.80	0*
Chest wheezy or whistling	0.80	0.53
Asthma in previous 12 months	0.96	0.76
Cold goes to chest usually	1.0	1.0
Cough and phlegm for 3 wk in previous 12 months	0.95	0*
Absence from school for 1 wk or more in previous 12 months	1.0	1.0

\* In each case, one marginal was zero, making Kappa an unreliable estimate of chance-corrected agreement.

testing in each of the 3 yr are shown in table 3. There is a slight excess of males over females in each year, and the predominant Caucasian ethnic characteristic of the sample is to be noted.

Previous studies have shown that certain factors other than outdoor air quality can be related to the incidence or prevalence of childhood respiratory disease (7, 10, 13). The distribution of these factors in each of the 4 original quadrants, and also in the additional group of schools in the industrial core that were added in Year 2, are shown in table 4. In this table, a smoker is one who smokes 1 or more cigarettes or cigars per day. The percentage with cough includes those with a positive answer to either of the questions: "Do you usually cough in the morning?" or "Do you usually cough during the day or night?" To simplify the presentation, only the results from Year 2 are shown. However, those from Years 1 and 3 are similar. The prevalence of these factors varied across the city and was highest in the industrial area, where the level of TSP was also the highest (table 1). A further, potentially confounding covariable was the prevalence of smoking by the children themselves. Because the age interval in the first year was between 7 and 10 yr of age, we did not expect to find many smokers. However, by the third year of the study, it might be expected that some of the older children would have commenced regular smoking. We therefore administered a smoking questionnaire to the children at the time of pulmonary function testing. The number of children in each age group who stated that they had smoked at least 1 cigarette in the last 4 wk is shown in table 5.

#### Quality Control

The repeatability of the respiratory symptom questions is shown in table 6, which

details the agreement statistics for each of these questions, both in terms of raw agreement and of chance-corrected agreement (Kappa). In certain cases, Kappa was an unreliable estimate of chance-corrected agreement, because one marginal of the  $2 \times 2$  table from which the Kappa was to be computed was zero. Kappa ranged from a substantial level of 0.56 to an excellent level of 1.0. The per-

centage of missing values by team for variables derived from the 4 pulmonary function maneuvers is shown in table 7. The values are shown for Year 1. The commonest reason for a pulmonary function value to be missing was that the child could not meet the required criteria for test acceptance. These results, therefore, give a comparison of ability of the 2 teams in obtaining successful tests for each test in each age group. The repeatabilities of the lung function measurements in Years 1 and 2 of the study are shown in tables 8 and 9. There were small but significant differences for several of the measurements (FVC,  $MEF_{50}$ ,  $MEF_{75}$ , MET, and VC) in Year 1 and to a larger extent in Year 2. The results for Year 3 are not displayed for sake of brevity, but they showed no significant differences. The product-moment correlation coefficients for certain of these variables are shown in table 10 for Year 1. These range from 0.97 for FVC to 0.14 for CV/VC. The reproducibility of these tests might have been affected by the presence of a respiratory infection during either the ini-

TABLE 7  
PERCENTAGE OF MISSING VALUES BY TEAM: YEAR 1

Variable	Team	Age (yr)						Total
		6	7	8	9	10	11	
FVC	A	0.0	1.0	0.4	2.1	0.3	2.8	1.0
	B	0.0	3.3	1.6	1.3	0.9	3.4	1.8
VC	A	33.3	12.5	5.1	7.5	1.0	0.0	6.4
	B	33.3	11.5	5.4	2.4	1.8	3.4	5.1
FRC	A	16.7	5.8	3.9	4.8	1.0	0.0	3.9
	B	16.7	10.4	5.0	1.5	1.3	3.4	4.4
CV	A	66.7	49.0	26.6	23.8	12.6	5.1	27.7
	B	33.3	37.4	24.2	14.3	9.0	20.7	21.2
$N_2$ difference	A	66.7	49.3	26.8	23.8	12.6	5.1	27.9
	B	33.3	38.5	24.2	14.0	9.0	20.7	21.3
Children tested, n	A	6	304	532	480	286	39	1,647
	B	6	270	501	456	223	29	1,485

Definition of abbreviations: CV = closing volume;  $N_2$  difference = increase in expired nitrogen concentration during phase III of single-breath nitrogen washout.

TABLE 8  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 1

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	216	2.04	0.41	2.07	0.41	-3.96	< 0.001
FEV <sub>1</sub>	216	1.87	0.31	1.86	0.31	1.33	0.190
$MEF_{50}$	215	2.33	0.62	2.14	0.59	3.57	< 0.001
$MEF_{75}$	211	0.99	0.36	0.94	0.32	3.45	0.001
MET	215	0.57	0.17	0.59	0.16	-3.13	0.002
VC	220	2.05	0.41	2.08	0.40	-3.30	0.001
FRC	210	1.19	0.31	1.19	0.29	0.13	0.895
CV/VC	166	0.134	0.09	0.12	0.078	1.42	0.158
$N_2$ diff	160	1.04	0.66	1.03	0.52	0.13	0.900

Definition of abbreviations: MET = midexpiratory time in seconds. For other definitions, see table 7.

TABLE 9  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 2

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	256	2.37	0.47	2.35	0.51	2.24	0.026
FEV <sub>1</sub>	256	1.91	0.36	1.88	0.39	2.66	0.008
MEF <sub>50</sub>	254	2.46	0.63	2.39	0.66	2.64	0.009
MEF <sub>75</sub>	254	1.05	0.34	1.03	0.35	1.49	0.138
MET <sub>75</sub>	256	0.59	0.16	0.60	0.19	-1.79	0.75
VC	255	2.39	0.47	2.36	0.49	2.37	0.019
FRC	253	1.32	0.33	1.31	0.34	0.37	0.713
CVVC	226	0.12	0.06	0.12	0.09	-0.13	0.897
N <sub>2</sub> diff	226	0.88	0.50	0.85	0.44	1.35	0.178

For definition of abbreviations, see tables 7 and 8.

tial or the repeat test. The repeatabilities of the lung function measurements were therefore reanalyzed, omitting from the analysis any test during which the presence of an upper or lower respiratory infection had been recorded. The results from this analysis are shown in table 11. Comparison with table 9 does not indicate that the reproducibility of the test was improved by the exclusion of current respiratory infections. In addition, for no variable was the product-moment correlation coefficient changed by the exclusion of respiratory infections.

### Discussion

This report outlines the background to the study that has been undertaken, the design of this study, and the methods that were used, and it describes the sample that was studied, both in terms of its characteristics and also in terms of important covariables. The design of the study was innovative in selecting schools within each of 4 quadrants of the city in expectation that these areas would show different levels of air quality. However, the area of the city with TSP levels greater than 60  $\mu\text{g}/\text{m}^3$  annual geometric mean was underrepresented when the air quality results from the first year were analyzed. This required the addition of

3 schools in the industrial core in the second year to achieve a gradient of air quality that one might expect to show an effect on the child's respiratory health. Financial constraints often dictate that air quality monitoring is done at the same time as the measurements of respiratory disease outcomes in children or in adults. However, without detailed prior information about the distribution of air quality gradients, modification of the design may be required during the course of the study, with the increased difficulty this might give in the analysis of the results. Random selection of schools within each quadrant was performed for this health study in the first year but not with the additional schools in the second year, because all the schools in the industrial core (that is, the area of highest particulate levels) were chosen for inclusion in the study.

The cooperation obtained from the Board of Education for the City of Hamilton and the parents of the children was excellent. We feel that the response rate in excess of 95% obtained in each year enables us to extrapolate any conclusions from the sample chosen to the total population of children at risk.

It was not surprising to find that the

distribution of covariables, which might influence the child's respiratory health, was not uniform across the city. In the examination of the relationship between levels of air pollutants and respiratory health, it is very important that any confounding effect of covariables be distinguished from the effect of air pollution itself. We have shown that the industrial area, which has the highest level of TSP, has also the highest prevalence of domestic smoking, parental respiratory symptoms, and gas cooking (22).

A further important consideration in the study of the effect of air quality on respiratory health is the previous mobility of the sample being studied. As table 4 shows, the proportion of children who had lived at their present address for less than 2 yr varied from 34.4% in the industrial core to 19.0% on the eastern part of the mountain. This difference would also have to be taken into account in any analysis of these results.

Cigarette smoking by the children themselves also becomes important in this particular age group as it can lead to respiratory disease. Tager and coworkers (23) showed that children's smoking habits must be taken into account when looking at any putative effect of parental smoking. Direct validation of the estimates of smoking obtained from our smoking questionnaire was not performed. However, the percentage of children admitting to smoking in the previous 4 wk does increase in the expected direction with increasing age. In addition, these data are comparable to those obtained by Brown and colleagues (24) in their survey of smoking habits in Canadian school children. We are therefore confident that these results do reflect the smoking habits of the children. However, the rate of 4.8% who had smoked in the previous 4 wk is unlikely to affect the interpretation of the results.

TABLE 10  
PRODUCT-MOMENT CORRELATION  
COEFFICIENT OF INITIAL AND REPEAT  
ESTIMATES OF PULMONARY  
FUNCTION VARIABLES

	Year 1	Year 2
FVC	0.97	0.86
FEV <sub>1</sub>	0.94	0.83
MEF <sub>50</sub>	0.78	0.74
MET	0.72	0.81
RV	0.40	0.43
CVVC	0.14	0.03

TABLE 11  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS  
RESPIRATORY INFECTIONS EXCLUDED: YEAR 1

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	159	2.02	0.41	2.04	0.41	-3.47	< 0.001
FEV <sub>1</sub>	159	1.66	0.30	1.64	0.30	0.97	0.37
MEF <sub>50</sub>	158	2.26	0.61	2.15	0.58	3.26	0.001
MEF <sub>75</sub>	158	1.00	0.34	0.94	0.32	2.99	0.003
MET <sub>75</sub>	158	0.56	0.17	0.58	0.16	-2.93	0.004
VC	162	2.03	0.40	2.05	0.40	-2.55	0.012
FRC	157	1.17	0.32	1.17	0.29	-0.31	0.76
CVVC	123	0.14	0.08	0.13	0.08	1.33	0.19
N <sub>2</sub> diff	120	1.01	0.59	1.06	0.50	-0.13	0.90

For definition of abbreviations, see tables 7 and 8.

The results of a number of quality control procedures were part of the study. The repeatability of the respiratory symptom questions was estimated only when those particular questions were asked from the randomly chosen questionnaires. We thought it important to compute chance-corrected agreement (Kappa), because the raw agreement, when the prevalence of a particular symptom is low, may give a false impression of good agreement, when in fact most of the agreement is due to chance alone. For 3 cases, Kappa could not be computed. On the other hand, by the criterion of Landis and Koch (25), agreement was substantial or better for the questions on asthma, colds to chest, and absence from school for more than 1 wk with a chest illness. It was only slightly less than substantial for the question on wheezing or whistling in the chest.

The ability of young children to perform pulmonary function maneuvers is shown in table 7. The forced expired maneuver was the one most successfully performed. In the older age groups, slow spirometry and the multiple-breath nitrogen washout were equally well performed. In contrast, the single-breath nitrogen washout had a failure rate in excess of 20%. This lack of success for this particular test did not improve in Year 2 and it has been our experience that the single-breath nitrogen washout test is a difficult maneuver to employ in large scale epidemiologic monitoring in children.

In tables 8 and 9, it can be seen that in Years 1 and 2 there were small but significant differences between the initial and repeat estimates of a number of the pulmonary function variables that were not due to the presence of a respiratory infection. The differences were not found to be significant, however, in Year 3. No significant differences were found between the initial and repeat estimates for the variables derived from the multiple- and single-breath nitrogen washout maneuvers. However, for these variables, the coefficient of variation was much greater than for the variables derived from the forced expired maneuver, and therefore the analysis was less powerful in being able to demonstrate a difference if one really existed. An additional measure of association, the correlation coefficient, was high for the variables (FEV<sub>1</sub> and FVC) derived from the forced expired maneuver, but was much less for those variables derived from the single-breath nitrogen washout. This low correlation reduces considerably the usefulness of

the single-breath nitrogen washout test because the amount of random variation may well obscure any true difference between samples.

In conclusion, we have described the design and execution of a study of the effects of environmental factors on the respiratory health of children within a single city. The random selection and high response rate have ensured that the sample is characteristic of the population of interest in the city. The accurate estimation of pollution exposure has required a more comprehensive network of air quality monitors than would normally be employed in a single city. The non-uniform distribution within the city of covariables, such as parental smoking and cough, has implications for the detection of the effects of suspended particulates and SO<sub>2</sub>, especially when those effects are likely to be small at current levels of these pollutants. If present, these effects are only likely to be detected with samples as large as the one that we have studied.

Pulmonary function testing, even in the youngest of children, had a high rate of success with the exception of the single-breath nitrogen washout. We were disappointed with the lower rate of success of this test, its greater degree of variability, and its lack of reproducibility. For these reasons, it was omitted from the Year 3 testing; we feel that its place in large scale epidemiologic testing has not been justified.

#### Acknowledgment

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Value  
tailed)

0.001  
0.37  
0.001  
0.003  
0.004  
0.012  
0.76  
0.19  
0.90

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Strachan, D.P., Elton, R.A. "Relationship Between Respiratory Morbidity in Children and the Home Environment" Family Practice 3: 137-142, 1986.

**SUMMARY:** The relationships between 12 features of the home environment and respiratory morbidity as reported by parents, and as recorded in general practice records, were studied in 165 children aged seven to eight years. Parental reports of wheeze, nocturnal cough and school absence owing to chest trouble were significantly more common among children with a family history of wheeze, and those from damp or mouldy housing. There were associations between coal fires and nocturnal cough and between an open window and wheeze. Multivariate analyses confirmed these associations to be independent of each other, and of the child's sex and seven other features of the home environment, including gas appliances and parental smoking. These same environmental variables were not consistently related to general practice consultations for wheeze or lower respiratory illness. Damp and mouldy housing, coal fires and open bedroom windows should be investigated further as potentially remediable causes of respiratory disease in childhood.

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# Relationship Between Respiratory Morbidity in Children and the Home Environment

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The relationships between 12 features of the home environment and respiratory morbidity as reported by parents, and as recorded in general practice records, were studied in 165 children aged seven to eight years. Parental reports of wheeze, nocturnal cough and school absence owing to chest trouble were significantly more common among children with a family history of wheeze, and those from damp or mouldy housing. There were associations between coal fires and nocturnal cough and between an open window and wheeze. Multivariate analyses confirmed these associations to be independent of each other, and of the child's sex and seven other features of the home environment, including gas appliances and parental smoking. These same environmental variables were not consistently related to general practice consultations for wheeze or lower respiratory illness. Damp and mouldy housing, coal fires and open bedroom windows should be investigated further as potentially remediable causes of respiratory disease in childhood.

The role of environmental factors in the causation of respiratory morbidity in childhood is poorly understood. Hitherto, interest has focussed on the possible hazards of parental smoking and nitrogen dioxide from gas cookers.<sup>1-4</sup> Respiratory illness is more common among children who live in neighbourhoods classified as urban local authority housing,<sup>5</sup> and there is a widespread conviction that housing in some way influences respiratory health.<sup>6</sup> This paper describes an exploratory study of the association between respiratory morbidity and various aspects of the home environment among seven- to eight-year-old children registered with a Scottish urban general practice serving an area of predominantly local authority housing.

## METHOD

In October 1983 a review was made of the general practice records of 198 children born in 1976 and registered with the West Granton Medical Group,

Edinburgh, Scotland. This large practice serves one of the most socially deprived areas of the city. Entries in the records with a mention of wheeze, rhonchi or 'bronchospasm' were termed wheezing episodes, and those with a record of cough, wheeze or breathlessness, or auscultatory signs in the chest, were termed lower respiratory tract illnesses. Coryza, pharyngitis and otitis media were excluded, but an isolated symptom of cough was considered as a lower respiratory illness.

In January 1984 a postal questionnaire was sent to the parents of the same 198 children, enquiring how many nights the child had been kept awake by coughing during the autumn term 1983, and how many days the child had lost from school during the same term owing to chest trouble. These were chosen as readily quantifiable measures of respiratory morbidity that are known to relate to asthma in childhood. The parents were also asked if their child had ever had attacks of wheezing (defined in the questionnaire as breathing making a high-pitched whistling sound) and, if so, whether there had been any attacks over the past two years. This first questionnaire made no reference to interest in the home environment.

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In April 1984 a further questionnaire was sent to the same parents enquiring about absence from school owing to chest trouble, and about nocturnal coughing and wheezing during the spring term 1984. Additional questions related to features of the family and home environment which were considered to be possible risk factors for respiratory disease in this age group. Twelve features were expressed as binary variables for analysis:

1. Family history of wheeze: any first degree relative who had ever had attacks of wheezing.
2. Family size of four or more: usually resident at the child's home address.
3. Other children in the family: usual residents under 16 years of age.
4. More than one person per room: usual residents, rooms excluding kitchen and bathroom but including living rooms.
5. Other persons sleeping in the child's bedroom.
6. Child's bedroom unheated: usually, over the past six months (winter 1983-4).
7. Child's bedroom window left open at night: usually, over the past six months (winter 1983-4).
8. Gas: any unvented gas-fired appliance in the house.
9. Coal: any coal-fired appliance in the house.
10. Parental smoking: any person smoking more than five cigarettes per day while in the house.
11. Damp: positive response to the question: is your home affected by damp?
12. Mould: positive response to the question: is your home affected by mould or fungus?

Univariate analysis was by  $2 \times 2$  contingency tables. The cross-product ratio (relative odds) was used to express the degree of association and significance levels were assessed by the chi-square test. Multiple logistic regression analysis was carried out using the GLIM statistical package.<sup>7</sup>

## RESULTS

Complete questionnaire data was received from the parents of 165 (83%) of the children. The response rates were similar for those with and without a record of wheeze in their general practice notes (89% and 81% respectively), suggesting minimal bias, at least with respect to

wheezing. Of these 165 children, 159 (96%) had general practice records complete for the past two years, and 143 (87%) were complete from birth.

### *Risk Factors in the Home*

All but 20 of the 165 children studied lived in local authority housing. Investigation of the associations among the 12 features of the home environment found that damp was significantly more common in homes where coal was burnt ( $\chi^2 = 7.32$ , 1 df,  $P < 0.01$ ), but not in homes using gas ( $\chi^2 = 0.56$ ). No significant association was found between a family history of wheeze and parental smoking or damp housing. Parental smoking was, however, more common in homes affected by damp ( $\chi^2 = 7.36$ ,  $P < 0.01$ ). Of the 50 homes in which damp was reported 66% were also said to have mould or fungus, but only two families reported mould in the absence of damp. The local environmental health department had received complaints of damp or mould from only five of these premises, although in all five cases dampness was confirmed after investigation by the department.

### *Associations with Parental Reports of Symptoms*

The parents of 33 children reported that their child had wheezed at some time. Of these, 31 (94%) were reported to have wheezed during the past two years and 21 (64%) during the spring term 1984. Of these 33 children 22 (67%) had attended their general practitioner at some time with wheeze, but only 16 (48%) had done so in the past two years. Furthermore, a wheezing illness was found in the records of 27 children whose parents reported they had never wheezed. The association of parental reports and general practice records of wheeze was therefore not as strong as might have been expected. The association between general practice consultations for lower respiratory illness and reported respiratory morbidity (school absence and nocturnal cough) was similarly weak.

The associations between parental reports of wheeze and the 12 features of the family and home environment were first assessed by univariate analysis (Table 1). Significant associations were noted with a family history of wheeze, an open bedroom window and damp or mould in the house. Multiple logistic regression analysis including the sex of the child and these 12 features as explanatory variables, with stepwise removal

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TABLE 1 Degree of association (expressed as relative odds of morbidity) between wheezing, school absence and nocturnal cough and 12 features of the home environment, based on reporting by parents

Risk factor	Prevalence (%)	Ever wheezed (20%) <sup>a</sup>	Autumn term 1983	
			School absence (25%) <sup>a</sup>	Nocturnal cough (49%) <sup>a</sup>
Family history of wheeze	48	2.6*	2.6*	2.8*
Family of 4 or more	82	1.0	0.7	1.0
Other children in family	84	1.1	0.6	0.7
More than one person per room	67	1.0	1.1	0.6
Others sleeping in bedroom	58	1.0	1.1	1.4
Bedroom unheated	60	1.5	1.1	1.6
Bedroom window open at night	28	3.6*	2.2	1.3
Gas appliance	69	0.9	0.8	1.0
Coal appliance	14	0.8	1.1	2.7
Parental smoking	75	2.1	2.9*	1.7
Damp	30	2.7*	3.0**	4.0***
Mould	21	3.9**	2.5*	4.8***

<sup>a</sup> Prevalence

\*P&lt;0.05, \*\*P&lt;0.01, \*\*\*P&lt;0.001

of terms, demonstrated that three factors independently contributed to the risk of wheeze: a family history of wheeze ( $\chi^2 = 4.35$ ,  $P < 0.05$ ), an open bedroom window ( $\chi^2 = 9.76$ ,  $P < 0.01$ ) and mouldy housing ( $\chi^2 = 9.88$ ,  $P < 0.01$ ). Given these factors, an unheated bedroom was of borderline significance ( $0.05 < P < 0.1$ ).

Absence from school owing to chest trouble during the two terms of the study was reported by the parents of 52 (32%) of the children, with 41 of these absent during the autumn term. Similar associations were found on univariate analysis during each term, suggesting that additional questions about the home environment had not biased the reported morbidity in the second questionnaire. The data relating to the autumn term 1983 are presented in Table 1. A family history of wheeze, parental smoking and damp or mouldy housing emerged as significant risk factors in univariate analysis. Multiple logistic regression analysis, using school absence during either term as the response variable, and the child's sex and the 12 features of the home environment as explanatory variables, demonstrated independent contributions from a family history of wheeze ( $\chi^2 = 10.39$ ,  $P < 0.01$ ) and mould ( $\chi^2 = 7.04$ ,  $P < 0.01$ ). When parental report of wheeze was included as a further explanatory variable, only family history remained as an independent risk factor, whereas the effect of wheeze was highly significant ( $\chi^2 = 31.4$ ,  $P < 0.001$ ).

The parents of 90 (55%) children reported that, at some time during the spring or autumn term, their child had been kept awake by coughing, 81 of these reporting cough during the autumn term. Again, the associations between environmental factors and reported symptoms were similar for each of the two terms in the study. Nocturnal cough during the autumn term was significantly associated with a family history of wheeze and damp and mouldy housing (Table 1). The association with coal-burning was of borderline significance ( $\chi^2 = 3.6$ ,  $0.05 < P < 0.1$ ). Multiple logistic regression analysis using nocturnal cough during either term as the response variable, and explanatory variables as before, demonstrated independent contributions from a family history of wheeze ( $\chi^2 = 9.93$ ,  $P < 0.01$ ), coal ( $\chi^2 = 4.67$ ,  $P < 0.05$ ) and mould ( $\chi^2 = 11.89$ ,  $P < 0.001$ ). When wheeze was included as a further explanatory variable, it made an independent contribution ( $\chi^2 = 11.73$ ,  $P < 0.001$ ) but family history, coal and mouldy housing remained significant risk factors for nocturnal cough ( $P < 0.05$  in each case).

In the multiple logistic regression analyses reported above, no significant interactions were found between the contributing factors, although with a population of this size, interaction effects would have to be large to reach statistical significance. Thus, the effect of environmental factors did not differ significantly between children with and without a family history of wheeze.

TABLE 2 Degree of association (expressed as relative odds of morbidity) between consultations for wheezing illness and lower respiratory illness and 12 features of the home environment, based on general practice records

Risk factor	Prevalence (%)	Wheezing illness		Lower respiratory tract illness	
		Age 0-5 (any) (22%) <sup>a</sup>	Age 5-7 (any) (13%) <sup>a</sup>	Age 0-5 (3 or more) (39%) <sup>a</sup>	Age 5-7 (any) (53%) <sup>a</sup>
Family history of wheeze	48	2.9 <sup>a</sup>	1.4	2.0	0.9
Family of 4 or more	82	3.0	0.5	1.2	1.2
Other children in family	84	1.7	0.6	0.5	1.2
More than one person per room	67	1.0	0.7	1.0	0.7
Others sleeping in bedroom	58	0.7	0.9	0.8	0.9
Bedrooms unheated	60	0.7	1.8	0.7	1.2
Bedroom window open at night	28	1.3	1.9	0.8	1.3
Gas appliance	69	1.8	1.0	0.9	1.2
Coal appliance	14	1.0	3.8	0.4	0.7
Parental smoking	75	3.4 <sup>a</sup>	1.6	1.3	0.8
Damp	30	2.1	1.7	1.2	0.8
Mould	21	2.2	1.5	1.0	1.0

<sup>a</sup> Prevalence

\*P&lt;0.05, \*\*P&lt;0.01, \*\*\*P&lt;0.001

*Associations with General Practice Consultations for Wheezing and Respiratory Illness*

The associations between the 12 features of the family and home environment and general practice consultations for wheezing illness and lower respiratory illness at different ages were assessed by univariate analysis (Table 2). Despite the strong associations of certain environmental features with reported morbidity (Table 1), these same features did not, overall, increase the probability of consultation with respiratory illnesses. When consultations for wheeze during the first five years of life were considered separately, there were significant associations with a family history of wheeze and parental smoking (Table 2). Frequent consultations for lower respiratory illness at ages up to four years did not result in a significantly greater probability of consultation with such an illness at age five to seven years ( $\chi^2 = 3.0$ ,  $0.05 < P < 0.01$ ). These observations would suggest that neither current respiratory morbidity nor long-standing patterns of consultation behaviour have a great influence on consultations for respiratory illness at this age.

The lack of overlap between reports of wheeze by parents and in the general practice records was exploited to investigate whether the association of reported morbidity and the home environment was accounted for by biased symptom reporting (discussed further below). Among the 132 children whose parents denied wheeze, a recorded consultation for wheeze was weakly associated

with parental smoking (odds 3.7,  $\chi^2 = 3.5$ ,  $0.05 < P < 0.1$ ), and damp housing (odds 2.5,  $\chi^2 = 3.1$ ,  $0.05 < P < 0.1$ ), suggesting that the association between symptoms and damp housing may not be entirely due to reporting bias.

## DISCUSSION

Many of the studies relating respiratory morbidity in childhood to environmental factors have relied upon reports of symptoms or diagnoses by parents. Reporting behaviour by parents may not be independent of the environment, particularly when the latter varies with socioeconomic status or is considered by the lay person to be detrimental to health. In a study of adult respondents, 43% of those living in areas of bad housing associated respiratory symptoms with their housing situation, whereas in areas of good housing only 10% did so.<sup>6</sup> Here, general practice records provided an additional data source against which it was hoped to verify parental reports of cough and wheeze. The correlation between reported morbidity and recorded consultations was not as close as might have been anticipated, and the associations which emerged, often at high levels of statistical significance, between the environment and reported symptoms were not found with general practice consultations for wheeze or lower respiratory tract illness.

This raises the possibility that reporting bias may account for some of the associations

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observed. Parents of symptomatic children may be more aware of potentially adverse environmental circumstances or parents who perceive their housing to be unsatisfactory may report symptoms of a different degree of severity than others. The design of the questionnaire survey to some extent guarded against such bias. The first questionnaire made no mention of interest in the home environment, enquiring only about symptoms. These symptoms were, nevertheless related to environmental variables derived from the second questionnaire. Furthermore, comparison of the responses to each questionnaire did not suggest that inclusion of questions about the home influenced reporting behaviour. Also, if reported data were excluded, damp housing was still associated (albeit at borderline significance) with consultations for wheeze. While it is acknowledged that reporting bias cannot be entirely excluded without objective physiological data, it is considered unlikely that the observed associations are entirely artefactual. Some doubt must be cast on the validity of general practice records as indices of lower respiratory morbidity in this age group.

The population studied was not representative of the city as a whole, but, by concentrating on an area of predominantly local authority housing, possible correlations between housing conditions and socioeconomic status were minimized. Furthermore, a number of other aspects of the home environment which might be expected to vary with social status were controlled in the analysis. In this population, highly significant associations emerged between damp and mould in the house and respiratory morbidity in children, at least as reported by their parents. On the grounds of the strength of the association, its consistency for all measures of reported morbidity studied, and its persistence when a number of possible confounding variables are controlled, damp, mouldy housing deserves consideration as a contributing cause of respiratory disease in children up to seven years old. Damp and mould are a common cause of complaint on aesthetic grounds. These potentially remediable conditions affect an estimated 2.5 million dwellings in the UK<sup>8</sup> and one-quarter of Scottish council houses.<sup>9</sup> The possibility that they might be a hazard to health should be more extensively investigated. In this preliminary enquiry, no independent assessment of damp or mould was made, but future studies could objectively assess both

relative humidity and the presence of fungal moulds or the prevalence of airborne fungal spores.

Others have reported an association between damp bedroom walls and wheeze in adults<sup>10</sup> and a correlation between relative humidity in the bedroom and respiratory symptoms in children.<sup>11</sup> Dampness encourages the growth of house dust mites, but it is unlikely that they are of aetiological significance in more than a few children with mite-sensitive asthma.<sup>12</sup> Most children who wheeze in early childhood eventually develop atopic reactions on skin-tests to common inhaled allergens,<sup>13</sup> and it is possible that fungal spores from mould may react with sensitized bronchi to cause both cough and wheeze. Exercise is a common precipitating cause of wheeze in the asthmatic child, but the available evidence suggests that a damp environment should have a protective effect.<sup>14</sup>

At the age of seven years, however, few children exhibit atopic skin test reactions,<sup>15</sup> and only half of the children with recent wheeze in this study were said to have attacks precipitated by exercise. Most episodes of wheeze in early childhood are thought to be precipitated by infection, and in at least half of cases a virus can be isolated.<sup>15</sup> It has been suggested that high relative humidity may encourage the transmission of viruses in droplet spray.<sup>16</sup>

The association of an open bedroom window with wheeze, but not with school absence or nocturnal cough, raises the possibility that this is a response by parents to the child's symptoms, rather than a factor of aetiological importance. In view of the likelihood that opening the window would raise the relative humidity of the room, such a response may be inappropriate.<sup>11</sup> The association of coal-fired appliances with cough is based on a small number of coal-fired homes but may warrant further consideration.<sup>10,17</sup> Although unvented gas appliances have been associated with respiratory symptoms in some studies of children of this age,<sup>3</sup> the relative risks quoted are small and might not be detected as significant in a study of this size. The data presented here do not support the hypothesis that greater condensation occurs in homes with gas cookers.<sup>4</sup> Parental smoking emerged as a less significant factor than might have been supposed,<sup>1,2</sup> but the analysis excluded the possibility that either smoking or gas fumes could account for the observed association between damp, mouldy housing and lower respir-

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atory morbidity in this sample of primary school-children.

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Anderson, H.R., Bland, J.M., Peckham, C.S. "Risk Factors for Asthma up to 16 Years of Age" Chest 91(6): 127S-130S, 1987.

SUMMARY: From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including feeding practices, and social and family factors were shown to have no effect on natural history.

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# Risk Factors for Asthma up to 16 Years of Age\*

## Evidence from a National Cohort Study

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From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including feeding practices, and social and family factors were shown to have no effect on natural history.

Much of the existing epidemiologic evidence about the etiology of asthma rests on prevalence and follow-up studies and there is a serious lack of population-based cohort data. The National Child Development Study (NCDS) originated in the National Perinatal Study<sup>1</sup> and went on to become a multipurpose cohort study of child development including health. While it was not designed specifically to study the epidemiology of asthma, it is nevertheless possible to obtain valuable information relating to the natural history of asthma. This article describes some of the findings from our analysis of NCDS data which have implications for the etiology of asthma.

### MATERIALS AND METHODS

The NCDS followed-up at ages seven, 11 and 16 all children in England, Scotland and Wales born during one week of March, 1958. At each follow-up, information about current or past asthma or wheezing illness was obtained as part of a structured questionnaire on medical and other topics administered to parents by health visitors. The wording of the asthma questions varied at each interview but it was nevertheless possible to classify subjects at each interview into three categories: no asthma or wheezing, previous asthma or wheezing but not in the past 12 months, and current asthma or wheezing (symptoms reported in the past 12 months). Based on these three possibilities at each of three interviews, 27 mutually exclusive natural history categories can be created. Some of these contain small numbers or are of limited clinical or epidemiologic interest, and so for the purpose of the present analysis a collapsed classification of six natural history categories was used.

These natural history categories were analyzed in relation to medical and social data collected at each of the follow-up medical examinations and home interviews. Factors that have previously been reported to be associated with asthma or wheezing were selected together with those considered likely to influence the natural history of asthma.

The overall association between a variable and the natural history category was tested using the Chi-squared test or one-way analysis of variance as appropriate. Where there was a statistically significant

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Law (Title 17 U.S.C. 101)—Lifetime Incidence of Asthma or Wheezing (n = 8,806)

Age at interview (yrs)	Asthma or wheezing at any time in past (percent)	
	Cross-sectional	Cumulative*
7	18.3	18.3
11	12.1	21.9
16	11.6	24.7

\*Using information from previous interviews

Table 2—Prevalence of Asthma or Wheezing in  
12 Months Preceding Interview (n = 8,806)

Age at interview (yrs)	Asthma or Wheezing in past 12 months (percent)	
	Cross-sectional	Cumulative*
7	8.3	8.3
11	4.7	10.7
16	3.5	11.1

\*Using information from previous interviews

overall association, the relative risks of each natural history category were calculated. The statistical significance of the relative risk was tested by calculating 95 percent confidence intervals.

### RESULTS

Data on asthma or wheezing were obtained at all three ages for 8,806 of the original NCDS cohort of over 15,000 children living in England, Scotland and Wales and available for follow-up at seven years.

The reported lifetime incidence of asthma or wheezing is shown in Table 1. Using data from all three interviews, a total of 24.7 percent of children had experienced asthma or wheeze by the age of 16 years. When questioned at age 16 years, however, the proportion reporting past asthma or wheeze was less than half this figure (11.6 percent). The prev-

Table 3—Prognosis of Asthma or Wheezing if Current  
(past 12 months) at Age 7 (n = 731)

Persistence of AW and age (yrs)	Percent of 7 year-olds who reported current AW
Current at 11	28.3
Current at 16	16.3
Current at 11 and 16	10.5
Current at 11 or 16	34.1
Not current at 11 or 16	65.9

Table 4—Natural History Categories (n = 8,806)

Category	Percent of sample
Never had asthma or wheezing	75.3
Onset before age 7 but not current at 7 or reported subsequently	8.6
Current at age 7 but not reported subsequently	5.5
Onset age 0 to 7 and also reported at 11 or 16	4.2
Onset age 8 to 11	3.6
Onset age 12 to 16	2.8

Table 5—Factors Predicting the Onset of Asthma or Wheezing

Predictive factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By age 7 not after	At age 7 not after	Age 0-7 and after	Age 8-11 onset	Age 12-16 onset
Perinatal							
Sex of child	<0.001	Boy: girl	1.1	1.2	1.4*	1.3*	1.4*
Mother's age	<0.001	15-19: 20-29 yrs	1.4*	1.5*	1.1	1.9*	1.7*
		15-19: 30+ yrs	1.6*	1.3	1.3	1.9*	2.0*
		20-29: 30+ yrs	1.2	0.9	1.1	1.0	1.2
Smoking in pregnancy	<0.001	Smoker: Non-smoker	1.3*	1.2	0.8	1.0	1.0
Region of child's birth	<0.01	North: Centre	0.7*	0.9	0.9	0.7	1.0
		North: South	0.8*	0.9	1.0	0.9	1.0
		Centre: South	1.1	1.0	1.0	1.2	1.0
Assessed at 7							
History of pneumonia	<0.001	Yes: No	2.0*	2.0*	4.3*	1.5	1.8*
Tonsillectomy/ adenoidectomy	<0.001	Yes: No	1.3*	1.2	1.2	1.2	1.4*
Eczema in 1st year	<0.001	Yes: No	1.2	1.4	5.4*	1.7*	1.5
Eczema after 1st year	<0.001	Yes: No	1.1	1.3	4.7*	1.3	1.7*
Eczema on Dr. exam.	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Hayfever or sneezing ever	<0.001	Yes: No	1.3	2.0*	7.1*	1.5	1.7*
Periodic vomiting or bilious attacks ever	<0.001	Yes: No	1.2*	1.4*	1.8*	0.8	1.4*
Periodic abdominal pain ever	<0.001	Yes: No	1.4*	1.3*	1.5*	0.9	1.4*
Assessed at 11							
Whooping cough ever	<0.001	Yes: No	1.2*	1.3*	1.4*	1.4*	1.4*
Eczema in past year	<0.001	Yes: No	1.2	1.2	4.2*	1.9*	1.7*
Hayfever or allergic rhinitis in past year	<0.001	Yes: No	1.0	1.2	5.2	2.2*	1.9*

\*P&lt;0.05

alence of current asthma was highest at seven years (8.3 percent) but had fallen to 3.5 percent at 16 years (Table 2). At each interview, the lifetime and current rates for the present cohort (those with data available at all interviews) were similar to those among subjects interviewed only once or twice. Of those with current symptoms at seven, 28 percent reported current symptoms at 11 years, 16 percent at 16 years and 11 percent at both ages (Table 3).

For the purpose of analysis, the 27 patterns of questionnaire response were collapsed into the six categories described in Table 4.

From an etiologic standpoint two types of relationship could be discerned. In the first, a given factor was assessed prior to the onset of asthma or wheeze, and could therefore be considered predictive. In the other, the order of occurrence of the factor and the onset of asthma or wheezing could not, from the data available, be shown to be predictive because the assessment of both factors was concurrent. Most factors found to be predictive are shown in Table 5 together with their relative risks. Any concurrent associations for these variables are also shown. Of the perinatal factors the most prominent was sex of the child and the mother's age at birth of the child. Multifactorial analysis was done to explore whether social class or breast feeding might explain this latter relationship, but this was not the case.

Of the factors assessed at seven or 11 years, the main ones predicting subsequent onset of asthma or wheezing were atopic conditions—eczema or allergic rhinitis—and (at

seven years only) periodic vomiting or abdominal pain. A history of pneumonia (at seven years) and whooping cough (at 11 years) were also predictive. Previous tonsillectomy or adenoidectomy reported at age seven years predicted onset in adolescence (though not when reported at 11 years).

Those factors which were concurrently associated with asthma or wheezing but not predictive are shown in Table 6. They mainly comprise upper and lower respiratory conditions but also include fits or convulsions in the first year (but not continuing into later life), enuresis, headaches and one adverse socioeconomic factor—sharing of one or more household facilities.

Those factors not associated with natural history are listed in Table 7. Notably, these included breast feeding, social class and a variety of indicators of socioeconomic circumstances and family stress.

Assessment of smoking in the household was inadequate, available only for the mother while she was pregnant and for both parents when the child was 16 years old. Smoking in pregnancy was associated only with an increased relative risk of asthma or wheezing during the early years of life and smoking by one or both parents reported when the child was 16 years was not related. At 16 years, the child's own smoking habit was unrelated to the presence of asthma or wheezing.

#### DISCUSSION

The National Child Development Study was not designed to examine the etiology of asthma and there are a number of

Table 6—Factors Concurrently Associated with Asthma or Wheezing but not Predictive

Concurrent factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By 7 not after	At 7 not after	0-7 and after	8-11 onset	12-16 onset
Assessed at 7 yrs.							
Household facilities	<0.008	Shared: not shared	1.1	1.5*	0.9	1.0	0.8
Whooping cough ever	<0.001	Yes: No	1.4*	1.2	1.4*	1.2	1.3
Throat/ear infections with fever >3 in past yr	<0.001	Yes: No	1.2	1.6*	1.4*	0.7	1.0
Running ears ever	<0.03	Yes: No	1.3*	1.3	0.9	1.0	1.2
Fits or convulsions in 1st year	<0.001	Yes: No	1.2	1.8*	2.7*	1.0	0.6
Wet by day after 3 yrs	<0.004	Yes: No	1.2	1.7*	1.0	1.5	1.2
Wet by night after 5 yrs	<0.001	Yes: No	1.5*	1.2	1.0	1.2	1.1
Assessed at 11 yrs.							
Household facilities	<0.05	Shared: not shared	1.0	1.4*	1.1	0.8	1.1
Recurrent throat/ear infections in past yr treated by Dr	<0.001	Yes: No	1.1	1.0	1.5*	1.7*	1.1
Discharging ears in past year	<0.07	Yes: No	1.2	1.3	1.8*	1.6	0.7
Tonsils/adenoids removed	<0.001	Yes: No	1.2*	1.3*	1.2	1.2	1.0
Eczema on examination (Dr.)	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Recurrent headaches or migraine past year	<0.001	Yes: No	1.2	1.1	1.6*	1.2	1.1
Recurrent vomiting or bilious attacks in past year	<0.09	Yes: No	1.0	1.5*	1.3	1.5	1.0

\*P&lt;0.05

inadequacies in the nature and timing of both the assessment of asthma and wheezing and of etiologic factors. Against this is the advantage that these data relate to a national representative sample and contain a substantial number of subjects followed-up over a long time.

By including all children with reported asthma or wheezing, however mild, the present analysis may have missed associations that relate only to more severe asthma or wheezing, which is the main concern in medical practice. The data do, however, allow a simple grading of severity and this is being analyzed at present.

Considering the logistics of such a national cohort study, the response rate for information about asthma or wheezing on all three occasions of 59 percent of the original NCDS cohort could be judged as successful. Nevertheless, this raises the possibility of bias, which has been examined in detail.<sup>2</sup> It would appear that this is unlikely to have biased our results for relative risks or incidence and prevalence estimates. At any particular age, the prevalence rates among children for whom we had linked data were similar to the rates among those not seen on each occasion. The 12-month prevalence rates observed at age seven years were similar to those of other population surveys which have included all wheezing illnesses.<sup>4,7</sup>

As far as etiology is concerned, the most important findings in this study are those relating to factors which predicted or did not predict the later onset of asthma or wheezing. Among the perinatal factors, a new and possibly important finding was that the risk of all natural history categories apart from persistent asthma or wheezing (reported on all three

occasions) was increased in children of mothers who were under 20 years of age at the birth of the child. This was independent of social class or breast feeding (which were

Table 7—Factors Not Found to Be Predictive or Concurrently Associated with Asthma or Wheezing

<b>Perinatal</b>	
	Birthweight
	Gestational age
	Parity
	Breast/bottle feeding
	Birth order
	Rank in family
	Social class
<b>Assessed at 7</b>	
	Crowding in household
	Number of children in household
	Tenure of accommodation
	Social class
	Separation from mother
	In local authority care
	Absence of one or more biological parents
	Previous measles
<b>Assessed at 11</b>	
	Previous measles
	Social class
<b>Assessed at 16</b>	
	Age at menarche
	Pubic hair rating (boys)
	Smoking of child
	Smoking of parents

unassociated with natural history anyway). Further analysis found that the effect of maternal age existed within the 16 to 19-year-old age group as well. This finding needs to be confirmed by other studies and we can offer no plausible theory to explain it.

The increased risk of asthma or wheezing in boys agrees with other studies,<sup>9</sup> though our results differ from most in that the effect of male sex did not diminish as the age of onset of asthma increased.

The question of whether breast feeding protects against childhood asthma is of great importance since, if true, it would offer insights into etiology and a method of prevention. The evidence is patchy, but a prospective study by Blair<sup>9</sup> found that asthma was more likely to persist in those who were bottle fed. Our results do not confirm this finding, nor was any other effect of infant feeding practice on natural history apparent.

The association between natural history of asthma or wheezing and other atopic conditions confirms the abundant evidence from other prevalence and case-control studies. Additionally, however, we have demonstrated that periodic abdominal pain or vomiting attacks are also predictive and that headaches or migraine are an important concurrent association, though falling just short of significance as a predictive factor. Such associations have also been observed in a separate prevalence study<sup>4</sup> and can no longer be regarded as speculative. We feel that elucidation of the nature of these associations is an important research priority.

The last group of factors found to predict the onset of asthma or wheezing in adolescence were chest infections (pneumonia and whooping cough) and this finding has an important bearing on the question of whether and how early childhood chest troubles may predispose to chronic lung disease in later life as indicated in a previous prospective<sup>20</sup> and retrospective study.<sup>21</sup>

There are various explanations for the associations we have observed. The report of pneumonia or whooping cough may have been a mistaken diagnosis for what was in reality asthma. Chest infection may have led to the later onset of asthma by creating some predisposition which remained latent until adolescence. Both chest infections and asthma may have a common environmental cause or may be the result of a common predisposition via some kind of general "chesty" tendency. Perhaps the asthmatic tendency itself could predispose to chest infections and in some circumstances the chest infection might be expressed prior to the first attack of asthma.

Data about wheezing symptoms and chronic productive cough have been collected from this same cohort at the age of 23 years. Analysis of this additional information should provide further important evidence concerning the origins of both asthma and chronic bronchitis.

### CONCLUSIONS

The National Child Development Study is an important source of nationally representative longitudinal data. While not specifically designed to study asthma, analysis of the data has elucidated a number of factors that predict the subsequent onset of asthma. These include male sex of the child, mother's age at child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and

periodic abdominal pain/vomitting attacks.

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## Occupational Asthma

Maire Chan-Young, M.B.,\* and Jean-Luc Melo, M.D.†

This article reviews recent developments in the study of occupational asthma and implications for the overall understanding of asthma. Occupational asthma is a clinical syndrome caused by many different agents. Contribution of studies of experimental inhalation challenge using occupational agents to the knowledge of asthmatic reactions and their mechanisms is discussed. Investigations in the occupational environment into predisposing factors and persistence or recovery after exposure to an allergic agent or nonspecific irritant are reviewed. Approaches to diagnosing asthma in the occupational environment and to assessing functional impairment and disability are outlined. Directions for future research are identified.

Studies in occupational asthma have provided considerable insight into the various etiologic factors, possible pathogenetic mechanism and, to a certain extent, the clinical course of asthma. For the purpose of this presentation, occupational asthma will be defined as asthma caused by a

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Fleming, D.W., Cochi, S.L., Hightower, A.W., Broome, C.V. "Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?" Pediatrics 79(1):55-60, 1987.

**ABSTRACT:** Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending daycare ( $P = .02$ , odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees ( $P = .005$ , odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day-care, 9% to 14% of the total burden of upper respiratory tract disease in this population was daycare related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood.

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## Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?

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**ABSTRACT.** Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending day care ( $P = .02$ , odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees ( $P = .005$ , odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day care, 9% to 14% of the total burden of upper respiratory tract disease in this population was day care related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood. *Pediatrics* 1987;79:55-60; upper respiratory tract infection, day-care attendance.

Infections of the upper respiratory system are the most common illnesses affecting children less than 5 years of age in the developed world. Although

these illnesses, including acute upper respiratory tract infection and otitis media, may occasionally progress to more severe disease, most often they are self-limited. Despite their relatively benign nature, however, upper respiratory tract infectious illnesses are important causes of childhood morbidity, and their treatment consumes a substantial portion of available health care resources.<sup>1</sup>

During the past decade, it has been demonstrated that risk of a number of childhood infections, including hepatitis,<sup>2</sup> diarrheal diseases,<sup>3</sup> and invasive *Haemophilus influenzae*,<sup>4</sup> is increased by day-care attendance. During this same time, the number of children younger than 5 years of age in the United States who are enrolled in day care has undergone a dramatic increase.<sup>5</sup> Although several studies have suggested that the risk of upper respiratory tract disease may be increased for some day-care attendees,<sup>6-8</sup> the importance of this association has not been well defined.

In this study, we examined risk factors for acquisition of infections of the upper respiratory system in children less than 5 years of age and specifically evaluated the role played by day-care attendance. Using population-based data, we determined the amount of illness attributable to this increasingly common childhood exposure.

### METHODS

A cross section of all households containing children less than 5 years of age in Atlanta was surveyed by telephone from mid-July through mid-September 1984.

### Sampling Procedure

Telephone numbers consisting of prefixes serving the study area and four randomly selected final

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digits were generated by computer. Every possible telephone number in the seven counties composing the metropolitan area (population 1.9 million) had an equal likelihood of being selected and called; no call-clustering techniques were used. Each number selected was called at least twice during business hours and at least six times during evenings and weekends before being discarded. Only households with children less than 5 years of age were enrolled.

#### Questionnaire Administration

Using a standardized questionnaire, trained interviewers obtained informed consent and then collected information from the guardian of the children in the household, preferably the mother. Data obtained included household demographic and socioeconomic characteristics, current maternal smoking history, and current breast-feeding and day-care attendance information for all children less than 5 years of age. All children within a given household were enrolled to ensure that our sample accurately represented all children in the study area with respect to household size and other related characteristics. A 15% sample of completed questionnaires was validated with a follow-up telephone call; no child's illness or day-care status was reclassified as a result of these calls.

#### Definitions

History of recent acute respiratory infection (cough, cold, or ear infection) was obtained directly from the child's guardian.<sup>4,7,9</sup> Because independent physician confirmation of illness was not required, we have used the term "ear infection" rather than otitis media to denote parental reported cases of infections of the ear. Criteria including antibiotic administration and physician visit were used if respondents needed clarification. We did not attempt to identify specific etiologic agents. Incidence of disease rather than duration of symptoms was assessed. To limit interviewer and respondent bias, illness history was elicited before parents were asked about day-care attendance. Children were considered case children if they had been ill with upper respiratory tract infection or ear infection at any time during the 2 weeks before the interview was conducted. Day care was defined as regular (>4 h/wk) supervised care of at least two unrelated children. Each child's day-care status was determined individually, based on enrollment at the time of interview. Part-time enrollment was defined as five to 39 hours' attendance per week and full-time as 40 or more hours per week.

#### Analysis

Two analyses of risk factors were undertaken,

one for children reported to have upper respiratory tract infection and the other for children reported to have ear infection. An automatic interaction detection program was used to assist in selection of variables for inclusion in an unconditional logistic regression model. Only associations that were biologically plausible were considered. We did not attempt to analyze or control for transmission of illness within households because we could not distinguish between primary and secondary cases. The number of children younger than 5 years in the household, a variable included in the model, may serve as a surrogate for intrafamilial spread. Final models were obtained by first putting all candidate variables into the model and then eliminating any variable that was not significant and whose elimination did not alter the odds ratio estimates of significant variables by more than 15%. Etiologic fractions among exposed groups (EF<sub>e</sub>) were calculated by the formula:  $EF_e = (\text{probability of disease in exposed} - \text{probability of disease in unexposed}) / (\text{probability of disease in exposed})$  and were standardized for the entire population by weighting the values from individual strata according to the percentage of the population represented by that strata. The disease probabilities used were those determined by the regression model.

#### RESULTS

A total of 3,952 households in the study area were surveyed. Of these, 3,387 contained no children younger than 5 years, 78 were unwilling to answer whether children were present and 487 contained at least one young child. Of these latter households, complete interviews were obtained for 449 (92%). Twenty-six percent of households (118) contained more than one child, and information regarding illness was collected for 575 children.

#### Upper Respiratory Tract Infection

Twenty-four percent of the children surveyed (139/575) were reported to have had an upper respiratory tract infection during the 2 weeks before the interview. The incidence of reported illness was divided equally by sex with 24% of both boys (75/307) and girls (64/268) affected. Race did not appear to be a significant risk factor; illness was reported for 23% of white children (96/421), 27% of black children (40/146), and 40% of children of other races (4/10). The frequency of upper respiratory tract infection did vary somewhat with age; incidence in children younger than 36 months was 27% (91/338), and in children 36 months or older, 20% (47/232).

On univariate analysis, children who attended

day-care facilities appeared to be more likely than children who did not attend to have had symptoms of an upper respiratory tract infection during the 2 weeks preceding the interview (32% [55/175] of attendees *v* 21% [84/400] of nonattendees;  $P = .01$ ,  $\chi^2$ ). A significant difference in risk between part-time and full-time attendance could not be demonstrated, although there was a suggestive trend in children younger than 36 months (42% [23/55] incidence in full-time attendees *v* 28% [11/39] in part-time attendees,  $P = .2$ , Fisher exact test). The type of day-care facility, ie, residential *v* nonresidential, and the length of time the child had been attending were not statistically associated with the likelihood of upper respiratory tract infection.

The association of day-care attendance with upper respiratory tract infection was further evaluated by logistic regression in a model that contained other variables considered to be possible risk factors for disease. These variables included family income, crowding (dichotomized at less than *v* equal to or more than one person per room), and number of children less than 5 years of age, maternal smoking, and child's race and age (dichotomized at 36 months). Current breast-feeding was included as a possible protective factor in children less than 6 months of age.

In this model, children who attended day care were significantly more likely than children who did not attend to have had a parent-reported upper respiratory tract infection during the 2 weeks before interview (odds ratio = 1.6,  $P = .02$ , Fig 1). In addition to day-care attendance, a second factor, maternal smoking, was also associated with increased risk of upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). The effects of day-care attendance and maternal smoking were independent of one another. Child's age, although itself not

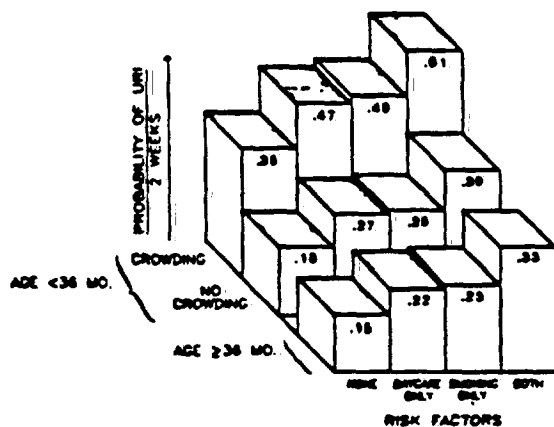


Fig 1. Probability of upper respiratory tract infection according to age, crowding, maternal smoking, and day-care status.

a risk factor (odds ratio = 1.2,  $P = .4$ ), did significantly modify the effect of a third variable, household crowding. Living in crowded conditions was significantly associated with upper respiratory tract infection in children younger than 36 months (odds ratio = 2.4,  $P = .02$ ) but not in children 36 months or older (odds ratio = 0.6,  $P = .4$ ). No statistically significant association with risk of upper respiratory tract infection was seen for family income, number of children less than 5 years, and child's race, and no protective benefit of breast-feeding could be demonstrated (Table 1).

Clustering of illnesses within households did not seem to significantly affect the association of upper respiratory tract infection with day-care attendance. This relationship in households with only one child less than 5 years of age was similar to that in households with two ill children (odds ratio = 1.73 *v* 1.72), and the prevalence of day-care attendance in ill children from households containing no other children less than 5 years was similar to that observed in children from households with another ill sibling (41% [35/85] *v* 40% [12/30]).

#### Ear Infection

Six percent (34/575) of children less than 5 years of age were reported to have had an ear infection during the 2 weeks before the interview. Ear infection was reported more often for boys than girls (7.2% *v* 4.5%), but this difference was not statistically significant. Black children and white children were affected equally (6.1%); none of the ten children of other races were reported ill. Compared with upper respiratory tract infection, the incidence of ear infection was more influenced by age. Incidence was 8.6% (29/337) in children 0 to 35 months of age and 2.1% (5/233) in children 3 or 4 years of age. Children with ear infection were significantly more likely than children without ear infection to have had upper respiratory tract infection symptoms during the preceding 2 weeks (65% [22/34] *v* 22% [116/535]; odds ratio = 6,  $P < .001$ , Fisher exact test).

Univariate analysis suggested that, as with upper respiratory tract infection, children attending day

TABLE 1. Variables Not Included in Final Upper Respiratory Tract Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.17
Race	1.1	.76
Breast-feeding	1.0	.98
Income (\$)		
0-19,999	1.0	
10-34,999	1.5	.14
≥35,000	1.0	.91

care were at increased risk for development of ear infection. For ear infection, however, only children who attended a day-care facility 40 or more hours per week could be shown to be at increased risk. This association with full-time attendance was present when either all children or only children younger than 36 months were evaluated (Table 2). Although the number of children with ear infection who attended day-care full time was relatively small, the type of day-care facility, ie, residential v nonresidential, and the length of time the child had been attending did not appear to be associated with increased risk of disease.

The association between full-time day-care attendance and ear infection was evaluated in a logistic regression model containing the same variables that were used for the upper respiratory tract infection analysis. Concomitant upper respiratory tract infection was not considered as a separate risk factor because this illness may, in many instances, represent an intermediate step between exposure to a risk factor and ear infection.<sup>8,10</sup> Clustering of ear infections within a household occurred only once and, thus, was not a factor in analysis. In the ear infection model, full-time day-care attendance was strongly associated with increased risk of ear infection (odds ratio = 3.2,  $P = .005$ ). Age was a second important predictor of disease, with children younger than 36 months at higher risk than children 36 months of age or older (odds ratio = 3.3,  $P = .02$ ). Among young children, as with upper respiratory tract infection, crowding was an important factor predicting disease (odds ratio = 3.4,  $P = .01$ ); in the older age group, data were insufficient to assess the effect of this variable (Fig 2). For ear infection, family income, number of children less than 5 years of age, maternal smoking, and child's race and breast-feeding status were not significantly associated with risk (Table 3). Two factors, maternal smoking and part-time day-care attendance, which were associated with the risk of upper respiratory tract infection, were not associated with the risk of ear infection. This finding may be due to the smaller numbers of children with ear infections and consequent lack of statistical power or

TABLE 2. Incidence of Ear Infection by Day-Care Attendance Status for All Children and Children 0 to 35 Months of Age

Day-Care Attendance Status	Incidence of Ear Infection (%)	
	All Children	0-35 Mo
Nonattendees	4.8 (19/395)	7.0 (17/244)
Part-time attendees	4.1 (3/73)	5.3 (2/38)
Full-time attendees	11.7 (12/102)	18.2 (10/55)
Status not available	(0/5)	(0/1)
Total	5.9 (34/575)	8.7 (29/338)

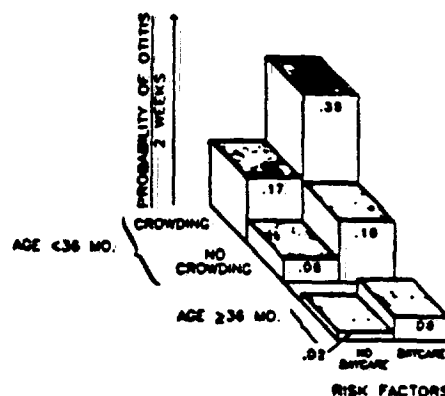


Fig 2. Probability of ear infection according to age, crowding, and day-care status.

TABLE 3. Variables Not Included in Final Ear Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.43
Maternal smoking	1.1	.82
Race	1.0	.93
Breast-feeding	1.9	.32
Income (\$)		
0-19,999	1.0	
20-34,999	0.9	.87
≥35,000	0.8	.73

alternatively to actual differences in risk factors for these two syndromes.

#### Attributable Risk

Perhaps the most meaningful measure of the amount of upper respiratory tract disease associated with day-care attendance is the etiologic fraction among the exposed children or  $EFe_{(day-care)}$ , which can be interpreted as the proportion of respiratory illness among children who attend day care that is directly related ("attributable") to this exposure.

In this study, the  $EFe_{(day-care)}$  for upper respiratory tract infection, adjusted for the other variables shown to be associated with upper respiratory tract infection, was 31%. Thus, approximately one third of upper respiratory tract infections in children who attend day care may be attributable to this specific exposure. The  $EFe_{(day-care)}$  for upper respiratory tract infections varied slightly by age and was 30% for children younger than 36 months and 33% for children 36 months of age or older.

For ear infections, the  $EFe_{(full-time day-care)}$  was 66%, standardized for the other variables shown to be associated with ear infection, and thus approximately two thirds of ear infection contracted by full-time day-care attendees may be directly re-

TABLE 4. Etiologic Fraction Among Exposed Groups ( $EFe_{day-care}$ ) and Population Attributable Risk of Upper Respiratory Tract Infection and Ear Infection Associated with Day-Care Attendance

Child's Infection and Age (Mo)	$EFe_{day-care}$	Children Attending Day-Care (%)	Population Attributable Risk (%)
Upper respiratory tract			
0-35	.30	29	9
≥36	.33	34	11
Ear infection			
0-35	.64	16	10
≥36	.68	20	14

lated to that specific exposure. The age-specific  $EFe_{(full-time\ day-care)}$  for ear infection was 64% for children 0 to 35 months of age, those at highest risk, and 68% for children 3 and 4 years of age.

The amount of upper respiratory tract disease in all young children that is directly related to day-care attendance (the etiologic fraction among the population, also called the population attributable risk) depends not only on the proportion of illness related to attendance but also on the proportion of children who attend. This latter figure is likely to depend on a variety of factors including geographic region, season of the year, and age of the children involved. In Atlanta, during the summer of 1984, the population attributable risk for day-care attendance varied between 9% and 11% for upper respiratory tract infection and between 10% and 14% for ear infection, depending on child's age (Table 4).

## DISCUSSION

Although more than 11 million children in the United States attend some form of day care,<sup>11</sup> estimates of risk have not been available for many of the illnesses to which these children are exposed, and the need for population-based studies has become increasingly apparent.<sup>11,12</sup> In particular, although the association between day-care attendance and infections of the upper respiratory system was suggested more than 35 years ago,<sup>13</sup> the contribution of day-care exposure to overall risk for these diseases has not been defined.

This study was designed to quantify the relation between day-care attendance and risk of childhood upper respiratory tract infections. Controlling for the effect of other risk factors, children in this cohort who were enrolled in day care were substantially more likely to have both upper respiratory tract infection and ear infection. Because these children were randomly selected from the general population, we could calculate that approximately

one third of upper respiratory tract infections among day-care attendees and two thirds of ear infections among full-time day-care attendees were directly related to attendance. Because data regarding the proportion of children in the population attending day-care facilities were also available, we were able to estimate that 9% to 14% of all upper respiratory tract infections and ear infections in children less than 5 years of age may occur as a result of day-care attendance, a figure generalizable to other areas to the extent that day-care attendance patterns in Atlanta are similar to attendance patterns elsewhere. These estimates provide a useful assessment of the influence of day-care attendance on the overall risk of upper respiratory tract infection in young children. Respiratory illness results in an estimated 17.4 million physician visits a year in the United States<sup>1</sup> and for otitis media alone, an estimated annual expenditure of more than \$2 billion.<sup>14</sup>

These percentages should be interpreted with appropriate caution. Having a child in day care may alter the likelihood that parents will notice and report illness in their children. This study determined a point estimate of risk based on parental reporting of illness during a 2-week period and, as such, should be viewed as only a first step in quantifying the effect of day-care attendance on the incidence of childhood upper respiratory tract infections. Nevertheless, the case definition based on parental reporting can be partially validated by the results of the analysis. If parents were reporting respiratory infections when no illness had occurred, one would not expect to find significant associations with crowding or maternal smoking. The substantial portion of upper respiratory tract infection linked to day-care attendance in this study suggests that it would be useful to determine whether specific etiologic agents may be particularly associated with this risk.

Additional studies that assess risk over season should be undertaken. For example, the risk of upper respiratory tract infection associated with day-care attendance calculated by this study may be a minimum estimate; day-care attendance may be more strongly linked with disease during the winter respiratory illness season when the likelihood of the introduction of upper respiratory tract infection into a day-care facility may be greater. Alternatively, a greater background incidence of viral infection during the winter might reduce the added risk associated with day-care attendance.

Several aspects of analysis other than the relation between upper respiratory tract illness and day-care attendance deserve comment. The similarity of the risk factor models for upper respiratory tract

infection and ear infection demonstrates the close association between these two illnesses and reaffirms the likely role of upper respiratory tract infections in the pathogenesis of ear infection.<sup>8,10</sup> The data regarding maternal smoking underscore the link between passive exposure to smoke and development of upper respiratory tract infection in children.<sup>14,16</sup> In this study, the proportion of upper respiratory tract infections in children of smoking mothers attributable to this exposure (34%) and the total population attributable risk (10%) were comparable to those calculated for day-care attendance.

As risk factors, however, there is a major difference between maternal smoking and day-care attendance. Whereas maternal smoking is totally preventable, day-care attendance is not. This difference highlights an increasingly obvious dilemma: child day care provides an irreplaceable service; yet, by its nature, it also results in enhanced transmission of infectious illnesses. The most practical approach to this problem—reduction of risk among those children who attend—rests on the assumption that differences in day-care facilities and children's exposures within those facilities may affect degree of risk. For diarrheal disease, this assumption seems warranted; risk has been shown to be influenced by a variety of specific day-care characteristics.<sup>3</sup> Whether the same is true for respiratory disease remains an open question. Identification of specific factors that are associated with increased risk of upper respiratory tract disease within day-care facilities should be a primary goal of future study.

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Martin, C.J., Platt, S.D., Hunt, S.M. "Housing conditions and ill health" British Medical Journal 294:1125-1127, 1987.

ABSTRACT: Lack of empirical evidence that living in damp houses has detrimental effects on health may partly be due to inadequate research. A preliminary study was therefore carried out of a random sample of council owned residences in a deprived area of Edinburgh, a respondent from consenting households being interviewed to obtain a profile of the physical and mental health of all adults and children. In addition, information was gathered about other factors that might be important, particularly smoking and selective bias in the allocation of tenants to houses. Independent measures of dampness were made by environmental health officers.

No conclusive effects of damp on the health of adults were identified. Nevertheless, children living in damp houses, especially where fungal mould was present, had higher rates of respiratory symptoms, which were unrelated to smoking in the household, and higher rates of symptoms of infection and stress.

Housing should remain an important public health issue, and the effects of damp warrant further investigation.

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## Housing conditions and ill health

CLAUDIA J MARTIN, STEPHEN D PLATT, SONJA M HUNT

### Abstract

Lack of empirical evidence that living in damp houses has detrimental effects on health may partly be due to inadequate research. A preliminary study was therefore carried out of a random sample of council owned residences in a deprived area of Edinburgh, a respondent from consenting households being interviewed to obtain a profile of the physical and mental health of all adults and children. In addition, information was gathered about other factors that might be important, particularly smoking and selective bias in the allocation of tenants to houses. Independent measures of dampness were made by environmental health officers.

No conclusive effects of damp on the health of adults were identified. Nevertheless, children living in damp houses, especially where fungal mould was present, had higher rates of respiratory symptoms, which were unrelated to smoking in the household, and higher rates of symptoms of infection and stress.

Housing should remain an important public health issue, and the effects of damp warrant further investigation.

### Introduction

The *BMJ* argued recently that the health implications of poverty, unemployment, and inadequate housing were not being emphasised strongly enough and made a plea for the formation of a public health alliance to highlight these issues.<sup>1</sup> Certainly, the role of housing conditions in the aetiology of illness appears to have received comparatively little attention since the decline of tuberculosis in the 1950s.

Most recent studies of housing conditions have concentrated on the relation between living in a damp house and respiratory complaints such as asthma<sup>2</sup> and wheeze.<sup>3,4</sup> Rising and penetrating damp provide the moist conditions conducive to germination of spores of mould fungi. Fungal spores, in turn, are believed to affect the respiratory tract by producing lesions in tissue, by forming saprophytic colonies on plugs of mucus, and by acting as allergens causing rhinitis, alveolitis, and asthma.<sup>5,6</sup> Some studies have suggested that ambient humidity influences the viability of viruses in droplet sprays.<sup>7,8</sup> The association between damp housing and health problems, however, is not clear cut, possibly being complicated by other factors known to affect health, such as smoking and poverty. A further serious flaw has been that the presence of damp has been reported by the householder or by the research team, casting doubt on the objectivity of the findings because of either the tenant's desire to get rehoused or bias in the experimenter.

This study was carried out in response to the concern of residents in a deprived area of Edinburgh about the possible effects of damp on their health. The preliminary study aimed at investigating the relation between damp housing and the physical and mental health of tenants and their children.

Edinburgh city is ringed by estates of council housing of varying quality and desirability, and the study area is regarded as one of the less (but by no means least) desirable in which to live (K Brown, unpublished master's dissertation, 1986). The area consists of

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only respiratory problems but other symptoms suggestive of infections and stress were more common in children in damp dwellings.

Respiratory problems may be due to the fact that the spores of many fungi act as allergens, sensitising mucous membranes and producing symptoms of wheezing, cough, fever, and general malaise in both atopic and non-atopic people.<sup>12</sup> Vomiting and diarrhoea in children in damp houses are harder to explain. Nevertheless, if mycotoxins in fungi were ingested their metabolites might give rise to the symptoms.<sup>13</sup> It seems probable that headache and "nerves" in the children may partly be related to the other symptoms or be a response to tension in the home; equally, however, they may be symptoms of emotional upset, possibly associated with recurrent symptoms, disruption of school and social activities, and the living conditions themselves.

Several studies have suggested an association between poor housing and health problems.<sup>14-16</sup> Acceptance of these findings and action on them, however, have been conspicuously absent, explanations including the financial and political implications of improving housing. At the scientific level most studies have been criticised on the grounds that the relation of ill health to poor housing could be confounded by other variables, such as low income, smoking, type of heating, overcrowding, housing allocation policies, and bias of experimenters or respondents, or both. This study, though based on fairly small numbers, has addressed such criticisms. It is plainly impossible to allow for all confounding factors; however, several alternative explanations of our findings appear to be unlikely.

Firstly, the sample was homogeneous with respect to social class and income. More than three quarters of respondents or their partners, or both, actually in employment were in manual occupations. Virtually all the households were on low incomes, and there were no income differences between those in damp and non-damp houses.

Secondly, the results show that certain aspects of the respondents' behaviour were not implicated. In particular, smoking made no contribution to children's respiratory symptoms. This is at variance with other studies,<sup>17-19</sup> but our sample was drawn from a social group with high rates of smoking,<sup>20</sup> and the adverse effects of parental smoking on children are largely confined to children under the age of 1 year.<sup>21</sup> Overcrowding and the number of children in the household were not contaminating factors; even after controlling for these factors significant effects for dampness remained. The use of calor gas fires in the home was not associated with either dampness or children's respiratory symptoms. Indeed, that the damp houses were mostly confined to particular streets makes it unlikely that the tenants themselves created the conditions which gave rise to damp.

Thirdly, issues of self selection and bias in the allocation of tenants to dwellings must be addressed—that is, that the "sick" may be more likely to move into poor housing or be allocated the worst properties. For the most part council tenants have little choice about where they will live and, though the low desirability of the study area inevitably leads to some self selection, it is by no means the least desirable of the council housing schemes in and around Edinburgh. Families living in damp houses were more likely to have come from poor conditions, but they were not more likely to have moved for health reasons. It was children, not adults, with poor health who were more likely to be living in damp houses; there was no evidence that behaviour problems in children were a factor in the allocation of families to particular houses. The only clear selection bias operating appeared to be of the infirm elderly being allocated better housing. There were no significant differences between damp and non-damp households in the length of time tenants had lived in their homes, and most had lived in the same house for more than five years.

As in most surveys, information about respondents' and children's health was reported by the respondent. Physical examination of all household members was beyond the scope of this study. Inevitably this raises questions about the possibility of reporting bias. Differential overreporting by those in damp houses would be manifested in respondents' reports of their own as well as their children's health, but it was clear that health differences were confined to children. Perhaps even more importantly, respondents who reported their homes to be damp were not more likely to report symptoms

either in themselves or in their children. The possibility of experimenter or respondent bias was minimised by having an independent survey of damp and not comparing data on dampness and health until the health data were coded.

Though it might be suggested that smokers may underreport symptoms such as coughing or wheezing, this was not the case in our study, where the highest rates of respiratory symptoms were found in heavy smokers. This, in turn, suggests that children's respiratory symptoms were not being underreported. Finally, there was no association between the respondents' mental state and the reporting of physical symptoms in children, suggesting that "psychologically distressed" mothers were not overreporting health problems in their children.

This study considered obvious confounding factors which might explain the findings and has gone a long way to ruling out selection and reporting biases. The findings appear to be robust and the association between living in a damp house and ill health in children cannot easily be attributed to other factors. Clearly, the number of households studied was fairly small and a larger investigation, using a double blind methodology, is warranted and is being planned. If our findings are replicated the public health implications will require urgent consideration. Improvements in the health of the population in the past 100 years have largely been a consequence of improved living conditions and thus a healthier home environment.<sup>22</sup> The early exposure to an adverse living environment is likely to increase vulnerability to illness in later life—particularly to the chronic respiratory diseases,<sup>23</sup> which are still a main cause of morbidity and mortality in Britain.

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SUMMARY: Previous epidemiologic studies have associated symptoms of chronic bronchitis and other respiratory diseases with the risk for lung cancer. To assess the possible precursor or premonitory role of these conditions for lung cancer among nonsmokers, a comparison of the prevalence rates of these conditions in 2 urban industrialized communities (Hong Kong and a Tokyo suburb) with a 300% difference in female lung cancer incidence rates was conducted. A community survey of 314 nonsmoking mothers and their children in Hong Kong, and 243 mothers and children in Japan showed that the prevalence of reported chronic cough and sputum symptoms was 10 or more times higher in Hong Kong than in Japan. The disparity in the rates of respiratory diseases/symptoms was most apparent in the comparison of children. Occupational exposure to dust or fumes and larger household sizes were found to be associated with higher levels of respiratory illnesses among the Hong Kong mothers. The much higher prevalence rates of respiratory symptoms among Hong Kong than among Japanese subjects correlated with each community's female lung cancer incidence rates of 27.1 versus 8.1/100,000, respectively.

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# A Comparison of the Prevalence of Respiratory Illnesses among Nonsmoking Mothers and Their Children in Japan and Hong Kong<sup>1,2</sup>

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## Introduction

A previous study on lung cancer among Hong Kong Chinese females found that patients with lung cancer were more likely to report a previous history of chronic cough or phlegm expectoration than were age-matched control subjects (1). These results were applied to those who had ever or never smoked, and a dose-response relationship was found between increasing years of experiencing these symptoms and risk for lung cancer.

The association of a previous history of respiratory diseases such as chronic bronchitis and pneumonia with lung cancer was first reported by Doll and Hill in their 1952 study on the etiology of lung cancer (2). Subsequently, other studies (3-5) also reported this association, although most did not segregate the effects of a past history of active smoking and the occurrence of these diseases.

Because Hong Kong Chinese females tend to have notably high lung cancer incidence rates, with a 1982 world age-adjusted incidence rate of 27.1 per 100,000 (6), a comparative study of females from a low incidence area such as Japan, with a world age-adjusted incidence rate of only 8.1 per 100,000 (7) for 1975-1979 in the Kanagawa Prefecture, might shed some light on this possible etiologic association. Both societies are racially similar and share a predominantly urban, industrialized environment. Yet their cultural habits and diets are sufficiently different to raise the possibility that their respective exposures to a variety of pollutants or protectors account at least in part for the 300% difference in their lung cancer rates.

The purpose of this cross-sectional study was to compare the prevalence rates of respiratory illnesses among children and mothers residing in 2 communities, one in Japan and the other in Hong Kong. Only subjects with no previous his-

**SUMMARY** Previous epidemiologic studies have associated symptoms of chronic bronchitis and other respiratory diseases with the risk for lung cancer. To assess the possible precursor or premonitory role of these conditions for lung cancer among nonsmokers, a comparison of the prevalence rates of these conditions in 2 urban industrialized communities (Hong Kong and a Tokyo suburb) with a 300% difference in female lung cancer incidence rates was conducted. A community survey of 314 nonsmoking mothers and their children in Hong Kong, and 243 mothers and children in Japan showed that the prevalence of reported chronic cough and sputum symptoms was 10 or more times higher in Hong Kong than in Japan. The disparity in the rates of respiratory diseases/symptoms was most apparent in the comparison of children. Occupational exposure to dust or fumes and larger household sizes were found to be associated with higher levels of respiratory illnesses among the Hong Kong mothers. The much higher prevalence rates of respiratory symptoms among Hong Kong than among Japanese subjects correlated with each community's female lung cancer incidence rates of 27.1 versus 8.1/100,000, respectively. *AM REV RESPIR DIS* 1988; 138:290-296

tory of active smoking were included. We wanted to know if differences found in their respective prevalence rates of respiratory illnesses would help explain the differing lung cancer incidence rates in the 2 populations. In addition, we wanted to know if these data could point to possible precursor respiratory conditions that might increase the individual's susceptibility to environmental carcinogens or that might indicate early premonitory symptoms since lung cancer is usually detected decades later.

## Methods

### Japanese Subjects

In July 1982, students from Grades 2 through 6 attending 2 public primary schools around the Tokyo area were surveyed. One school was located at the Suganami-ward in Tokyo and the other in Aikawa in the Kanagawa Prefecture, which is located about 50 kilometers west of Tokyo. The mothers of the surveyed children were also studied. These subjects were chosen from these districts because they would be representative of Japanese living in urban and rural environments in Japan. The Suganami-ward is a typical urban residential area with several heavily traveled roads traversing the district. The Aikawa area is characteristically rural without major factories and heavily traveled roads.

The response rate was 99.6% for the 457

children and 88.2% for their 403 mothers/guardians. Out of this sample, the following data were not included in this analysis: incompletely answered questionnaires ( $n = 38$ ), guardians who were not mothers of the children ( $n = 11$ ), any who reported a previous history of active smoking ( $n = 68$ ), and, in situations where 2 or more children from the same family were surveyed and attended the same school ( $n = 95$ ), only 1 of the children was randomly selected. Thus, the results from 243 mother-child pairs were analyzed for this study.

### Hong Kong Subjects

A government-subsidized primary school in the Ngau Tau Kok area of the Kwun Tong

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<sup>2</sup> Supported by Monbusho International Scientific Research Program and the Hong Kong Anti-Cancer Society.

TABLE 1  
AGE DISTRIBUTION AMONG MOTHERS

Age (yr)	Hong Kong		Japan	
	(n)	(%)	(n)	(%)
< 30	18	5.7	13	5.4
31-35	99	31.5	79	33.1
36-40	123	39.2	87	36.4
41-45	39	12.4	48	20.5
46-50	27	8.6	10	4.2
≥ 51	8	2.5	1	0.4
Unknown			4	
Total	314		243	
Mean age*	37.8		39.3	

\* *t* test, *p* value = 0.412

district of Hong Kong was selected in cooperation with the local government's Department of Education to represent subjects from a working class neighborhood. The site is surrounded by public housing in high-rise buildings and by small stores, and is within a few blocks of the small- and medium-sized factories that are common in this district.

Initially, 2 classes from each grade of 2 to 6 were planned for the study since each class averaged 36 students, and these numbers would approximate the age and sex distribution of the Japanese subjects. However, after data collection began, it was realized that some students in different classes were siblings, so an additional class in Grade 4 was included in the study. Thus, a total of 11 classes, i.e., 390 children and mothers were contacted for the study. The response rate for the return of the questionnaire was 100% for the children and 97% for their mothers/guardian (11 did not return the questionnaire). Using the same inclusion criteria as those for the Japanese subjects, 314 mother-child pairs were included in this analysis. To simulate the summer weather conditions of the Japanese collection time, the survey was conducted from May 20 to 30, 1985. The mean temperature and humidity in Hong Kong during the data collection period was 27° C and 81% humidity. The same data for Tokyo during July 1982 was 22° C and 77%, respectively. The Hong Kong data were collected in late May instead of July because the students would be off for summer vacations and thus not accessible.

#### Data Collection Forms

A modified version of the questionnaires originally developed by the American Thoracic Society Division of Lung Disease (ATS-DLD) (8) and the British Medical Research Council (BMRC) (9) to survey the prevalence of respiratory diseases was used. Questions were asked on the occurrence of the following: chronic cough or phlegm of ≥ 3 months duration (to eliminate those associated with acute upper respiratory tract infections), bronchitis, pneumonia, asthma, tuberculosis, allergic rhinitis, and other chest diseases.

The version for the children also included

TABLE 2  
AGE DISTRIBUTION AMONG CHILDREN

Age (yr)	Hong Kong		Japan	
	(n)	(%)	(n)	(%)
6	0		11	4.5
7	10	3.2	44	18.1
8	46	14.6	20	8.2
9	54	17.2	45	18.5
10	80	25.5	29	11.9
11	48	15.3	82	33.7
12	67	21.3	12	4.9
13	9	2.9	—	
Total	314		243	
Mean age*	10.1		9.4	
Girls, %†		48		46

\* *t* test, *p* value = 0.0001† *t* test, *p* value = 0.586

questions on sources and amounts of passive smoking exposure, and whether the child participated in home cooking activities. These questionnaires were distributed to the children at school and taken home with instructions that it be answered for the child by the mother or female guardian.

The version for the mothers included more detailed questions on cooking activities, active smoking history, and exposure to dust or fumes in the workplace. These questionnaires were distributed to the children at school with instructions that they should take them home for their mothers to fill out.

#### Data Analysis

The data collected in the questionnaires were coded and then processed by computer using the SPSS-X statistical package. Because the questionnaire asked about respiratory symptoms (i.e., cough, sputum, wheezing) and respiratory diseases (i.e., pneumonia, allergic rhinitis, bronchitis, asthma, tuberculosis), both were covered under the term "respiratory illnesses." These terms are distinguished

in this study because "respiratory symptoms" is a lay term that is easier for the subjects to identify with, whereas "respiratory diseases" would mean that a physician had diagnosed such a condition.

Analysis of the data included descriptive, comparative, and analytical work. In comparing the results between subjects from Hong Kong versus those from Japan, *t* tests or chi-square tests were usually done to estimate the statistical significance of the findings. Analysis on the relationship of multiple illnesses per person and various exposure categories utilized Pearson's goodness of fit test. A test for linear trend in the proportions was done when dose-response relationships were suggested (10). To statistically assess the risk among the exposed group versus the unexposed group, the following were calculated: relative risks as the ratio of these 2 proportions, attributable risk as the percentage of the overall risk in the exposed group, and the population-attributable risk as the difference in risk among the whole population (which we assume the entire sample represented) and the risk in the unexposed group (10).

#### Results

The age distribution of the 314 Hong Kong Chinese mothers and 243 Japanese mothers is shown in table 1. The Hong Kong Chinese mothers tended to be slightly younger, with a mean age of 37.8 versus 39.3 yr among the Japanese mothers, but these differences were not statistically different (*t* test, *p* value = 0.41). On the other hand, the 314 Hong Kong school children were slightly older than their Japanese counterparts (table 2), with the mean age of the former being 10.1 yr and that for the latter being 9.4 yr, which was statistically significant (*t* test, *p* value = 0.0001). The sex ratio for the children was not significantly

TABLE 3  
PREVALENCE OF SELF-REPORTED RESPIRATORY ILLNESSES AMONG NON-SMOKING MOTHERS

Respiratory Symptom/Disease	Prevalence (%)		
	Hong Kong (n = 314)	Japan (n = 243)	Chi-Square <i>p</i> Value
Chronic cough ≥ 3 months, %	5.7	0.4	0.006
Chronic phlegm ≥ 3 months, %	8.0	0.4	0.000
Cough and phlegm ≥ 3 months, %	3.2	0.4	0.0197
Cough or phlegm ≥ 3 months, %	10.5	0.4	0.0026
Bronchitis, %	7.6	5.8	0.3823
Ever had pneumonia, %	1.0	2.9	0.0897
Ever had asthma, %	1.3	2.9	0.1785
Ever had tuberculosis, %	1.6	2.1	0.6817
Ever had allergic rhinitis, %	11.5	12.4	0.7498
Ever had other chest diseases, %	0.3	1.2	0.2041
≥ 1 of the above chest illnesses, %	24.8	20.9	0.7054
Chest illnesses per sick mother, mean n	1.49	1.29	0.137*

\* *p* value by *t* test

TABLE 4  
PREVALENCE OF RESPIRATORY ILLNESSES AMONG CHILDREN  
AS REPORTED BY THEIR MOTHERS

Respiratory Symptom/Disease	Prevalence (%)		Chi-Square p Value
	Hong Kong (n = 314)	Japan (n = 243)	
Cough $\geq$ 3 months, %	7.0	0.4	0.0001
Phlegm $\geq$ 3 months, %	9.2	0.4	0.0000
Cough and phlegm, %	3.5	0	—
Cough or phlegm, %	12.8	0.8	0.0000
Cough or phlegm, yr/person	4.7	3.5	0.742*
Wheezing $\geq$ 3 months, %	7.6	1.7	0.0013
Wheezing, yr/person	4.8	6.8	0.180*
Ever had allergic rhinitis, %	9.2	11.1	0.4854
Ever had pneumonia, %	8.0	0	—
Ever had asthma, %	8.3	10.7	0.3304
$\geq$ 1 of the above chest illnesses, %	25.2	18.7	0.066
Chest illnesses per sick child, mean n	1.96	1.31	0.0001*

\* p value by  $\chi^2$  test

different for the 2 groups, with 48% of the Hong Kong children and 46% of the Japanese children being girls ( $t$  test,  $p$  value = 0.59).

The prevalence rates among mothers reporting a previous history of respiratory illnesses is shown in table 3. Among Chinese mothers, 5.7% ( $n = 18$ ) reported a previous history of chronic cough, and 8.0% ( $n = 25$ ), a history of chronic phlegm expectoration lasting 3 or more months. This contrasted with only 1 Japanese mother (0.4%) who reported having both such symptoms. For the other respiratory diseases, the prevalence rates between the 2 groups did not reach statistical significance ( $p \leq 0.05$ ). In general, there was a tendency for more Hong Kong mothers to report a previous history of chest problems (24.8 versus 20.9%); among those who had such diseases, Hong Kong mothers had more illnesses per person (1.49 versus 1.29) than did Japanese mothers. There was no relationship between the prevalence rates of respiratory illnesses and age of the mother in either population (chi-square,  $p$  value = 0.236 for Hong Kong mothers and 0.274 for Japanese mothers).

The prevalence of respiratory illnesses among children was similar to that of their mothers (table 4). One (0.4%) Japanese child was reported by the mother to be suffering from chronic cough, and another (0.4%) was reported to have chronic phlegm, whereas among the Hong Kong children these percentages were 7.0% ( $n = 22$ ) and 9.2% ( $n = 29$ ), respectively. When the 2 symptoms were combined, 12.8% ( $n = 40$ ) of the Hong Kong children had one or both symptoms, whereas this was true for only 0.8% ( $n = 2$ ) of

the Japanese children. All of these differences were statistically significant.

Among the other respiratory illnesses for the children, those in Hong Kong had statistically higher frequencies of wheezing (7.6 versus 1.7%) and pneumonia (8.0 versus 0%) than did their Japanese counterparts. The reported rates for allergic rhinitis and asthma were not statistically different for the 2 groups.

In the summary measurements, 25.2% of the Hong Kong children had one or more of the surveyed respiratory illnesses versus 18.7% among the Japanese children ( $p = 0.066$ ). Moreover, among those with such illnesses, the former group had a significantly larger mean number of problems per child (1.96) than did the latter (1.31).

The distribution of multiple illnesses within a single individual in the 2 areas is shown in table 5. Hong Kong mothers

TABLE 6  
RELATIONSHIP BETWEEN THE FREQUENCY  
OF RESPIRATORY ILLNESSES BETWEEN  
MOTHER-CHILD IN HONG KONG  
AND IN JAPAN\*

Illnesses per Child (n)	Illnesses per Mother (n)		
	0	1+	Total
<b>Hong Kong</b>			
0	186	48	234
1+	49	30	79
Total	235	78	313
Relative risk = 1.85†			
<b>Japan</b>			
0	157	33	190
1+	28	15	43
Total	185	48	233
Relative risk = 2.00‡			

\* The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq$  3 months, phlegm  $\geq$  3 months, wheezing, pneumonia, asthma, allergic rhinitis, bronchitis, TB, and other chest diseases.

† Pearson's correlation coefficient, 0.18;  $p$  value = 0.008.

‡ Pearson's correlation coefficient, 0.17;  $p$  value = 0.005.

and children consistently had higher percentages of such individuals than did the Japanese. This discrepancy was most apparent among the children, with 24 Hong Kong children (7.7%) having 3 or more respiratory illnesses versus only 1 Japanese child (0.4%) with such a history, and a comparison of their mean number of illnesses per child was highly significant ( $p = 0.0001$ ).

The frequency of illnesses in the mothers was related to that reported for their children as shown in table 6. In both populations, mothers who reported one or more respiratory illnesses for themselves were about twice as likely to report such illnesses in their children. Pearson's goodness of fit test showed this relationship to be highly significant.

TABLE 5  
FREQUENCY OF MULTIPLE RESPIRATORY ILLNESSES AMONG MOTHERS AND  
CHILDREN IN HONG KONG AND JAPAN

Illnesses per Mother*	Hong Kong Mothers		Japanese Mothers		Illnesses per Child†	Hong Kong Children		Japanese Children	
	(n)	(%)	(n)	(%)		(n)	(%)	(n)	(%)
0	235	75.1	185	79.4	0	234	74.8	190	81.5
1	54	17.3	39	16.7	1	45	14.4	30	12.9
2	14	4.5	4	1.7	2	10	3.2	12	5.2
3	7	2.2	5	2.1	3	11	3.5	1	0.4
4+	3	0.9	—	—	4+	13	4.2	—	—
Total	313	100	233	99.6‡		313	100.1‡	233	100
Mean	0.37		0.27			0.68		0.24	

\* The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq$  3 months, phlegm  $\geq$  3 months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

† The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq$  3 months, phlegm  $\geq$  3 months, wheezing, pneumonia, asthma, allergic rhinitis.

‡ Due to rounding off, the total sum was not 100%.



TABLE 7  
RELATIONSHIP OF OCCUPATIONAL DUST OR GAS/FUME EXPOSURE WITH  
RESPIRATORY ILLNESSES AMONG HONG KONG MOTHERS\*

Exposure at Work	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Dust				
No exposure	246	55	22.4	1.00
Mild	39	12	30.8	1.38
Moderate	25	9	36.0	1.61
Severe	4	2	50.0	2.23
Total exposed	68	23	33.8	1.51
Gas				
No exposure	278	63	22.7	1.00
Mild	23	9	39.1	1.72
Moderate	11	5	45.5	2.00
Severe	2	1	50.0	2.20
Total exposed	36	15	41.7	1.84

\* Linear trend  $p$  value  $\leq 0.05$ . Pearson's correlation coefficient significance  $p$  value presence and absence of illnesses: dust = 0.017, gas = 0.007. Exact number of illnesses: dust = 0.007, gas = 0.0008.

† The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq 3$  months, phlegm  $\geq 3$  months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

TABLE 8  
COMPARATIVE PROFILES OF HONG KONG AND JAPANESE  
MOTHERS AND CHILDREN

Lifestyle Variable	Hong Kong		Japan		Chi-Square p Value
	(n)	(mean)	(n)	(mean)	
Mother currently works outside the home	106	33.9%	88	28.0%	0.138
Father currently smokes	110	35.6%	146	80.1%	0.0000
Home has ventilated cooking*	251	79.9%	192	79.2%	0.789
Mean household size	314	5.31	243	4.54	0.0007†

\* Cooking area has electric ventilating fan or cooking hood.

†  $p$  value by  $t$ -test.

To understand the role of occupational exposures, the Hong Kong mothers were asked in the questionnaire whether they had ever worked for a year or more in places where they were exposed to noticeable levels of dust/smoke or gases/fumes, the degree of such exposure, where such exposure occurred, and what they did. Analyses of all the variables showed that the frequency of respiratory illnesses among Hong Kong mothers was highly related to their reports of previous exposure to dust or gas fumes (table 7) in the workplace.

Overall, some 21.7% ( $n = 68$ ) of the total sample of Hong Kong mothers reported a previous history of occupational exposure to dust, and 11.5% ( $n = 36$ ) to gas/fumes. The percentages of exposed mothers with one or more respiratory illnesses increased proportionately with the degree of reported severity of exposure to such air pollutants in a dose-response manner. Among those exposed to severe levels of either pollutant, the attributable risk was calculated to be

55%. Gas fumes seemed to exert a larger effect than did dust, as the attributable risk was 45.6% for the former versus 33.8% for the latter.

Although the same questions were not asked in the Japanese survey, data on Japanese mothers currently employed in dusty industries such as mining showed no relationship with their prevalence of respiratory illnesses. In addition, when comparing the lifestyle profiles of the 2 populations (table 8), it can be seen that mothers in Japan were less likely to work outside the home, so that their likelihood of being exposed to such occupational exposures would be less than that of the Hong Kong mothers.

In terms of possible sources of indoor air pollutants in the home, the data did not help explain the discrepancy in prevalence rates in the 2 populations. Some 60% of the Japanese fathers were current smokers versus only 36% of the Hong Kong fathers. Although cooking styles are greatly different between the 2 populations, with Chinese cooking methods more likely to produce cooking fumes because of the stir-fry method, the percentages of kitchens with mechanical ventilation fans/hoods was the same in both populations, i.e., 79 to 80%.

It was interesting to note that the mean household size was statistically different ( $p = 0.000$ ), with Hong Kong families averaging 5.31 persons versus 4.54 persons in Japan. The effects of family size on the frequency of respiratory illnesses are shown in table 9. There was a tendency for Hong Kong mothers living in larger households to report more respiratory illness than those living in smaller ones. However, such was not the case for the Japanese mothers. Moreover, among the Hong Kong mothers, no relationship was found between household density, i.e., the total number of people in the family

TABLE 9  
RELATIONSHIP OF FAMILY SIZE TO RESPIRATORY ILLNESSES  
AMONG HONG KONG AND JAPANESE MOTHERS\*

Household Size	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Hong Kong				
Small, $\leq 4$	100	22	22.0	1.00
Medium, 5 to 6	155	37	23.9	1.09
Large, 7+	59	19	32.2	1.46
Total	314	78	24.8	
Japan				
Small, $\leq 3$	29	5	17.9	1.00
Medium, 4 to 5	175	40	22.9	1.28
Large, 6+	40	9	22.5	1.26
Total	243	54	22.2	

\* Pearson's correlation coefficient significance and  $p$  values. Presence and absence of illnesses in Hong Kong:  $r = 0.024$ ,  $p = 0.33$ ; in Japan:  $r = 0.025$ ,  $p = 0.36$ . Exact number of illnesses in Hong Kong:  $r = 0.076$ ,  $p = 0.09$ ; in Japan:  $r = 0.034$ ,  $p = 0.30$ .

† The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq 3$  months, phlegm  $\geq 3$  months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

TABLE 10  
RELATIONSHIP OF HOUSEHOLD DENSITY WITH RESPIRATORY  
ILLNESSES AMONG HONG KONG MOTHERS\*

People per Room (n)	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Low, $< 2.49$	81	20	24.7	1.00
Medium, 2.5 to 3.5	105	23	21.9	0.89
High, $> 3.5$	128	35	27.4	1.11
Total	314	78	24.8	

\* Pearson's correlation coefficient and p values: presence and absence of diseases:  $r = 0.031$ ,  $p = 0.29$ ; exact number of diseases:  $r = 0.008$ ,  $p = 0.44$ .

† The presence of the following respiratory diseases unrelated to cold/flu: cough  $\geq 3$  months, phlegm  $\geq 3$  months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

divided by the number of rooms they occupied, and the frequency of respiratory illnesses (table 10). The Japanese data did not contain information on household density for comparative analysis.

#### Discussion

The findings of this preliminary epidemiologic study on the prevalence of respiratory illnesses among never-smoked mothers and children in Hong Kong and Tokyo suggest that such illnesses are much more common in Hong Kong. Hong Kong subjects were 10 or more times more likely than their Japanese counterparts to report symptoms of chronic cough and phlegm expectoration exceeding 3 months duration.

The differences in reported frequencies of respiratory illnesses were greatest in the comparison of school children. Hong Kong children were 4.5 times more likely to have had a previous history of wheezing, and 8 times more likely to have had pneumonia than were Japanese children. Overall, 25.2% of the Hong Kong children versus 18.7% of the Japanese children had one or more of the surveyor chest illnesses, and their mean numbers of chest illnesses per sick child were 1.96 and 1.31, respectively. All of these differences were statistically significant, with the comparison of those with chest illnesses of borderline significance ( $p = 0.066$ ).

We feel that the interpretation of these findings must be viewed in light of the degree of medical knowledge of the 2 populations. For a mother to report that she or her child had suffered from such diseases as bronchitis, pneumonia, asthma, tuberculosis, or allergic rhinitis, she would have had to have been told by a doctor of such a diagnosis/description of the problem. Because doctor-patient communication is poor in Hong Kong, and patients are frequently not told the diagnosis nor the names of the drugs that are prescribed, the knowledge/usage of

such medical terms among the population would be infrequent. This would be especially true among the working-class mothers whose average educational attainment is primary school only (11). Thus, these illnesses, which we have labeled as "respiratory diseases," would tend to be underreported in the Hong Kong population. On the other hand, such common descriptive terms as cough, phlegm expectoration, and wheezing are well understood by all, and thus the survey was able to reflect a more accurate recording of the prevalence of these symptoms.

Evidence for the fact that the greater unfamiliarity with medical terms among the Hong Kong mothers seemed to influence their reported frequencies is reflected in the unrealistically low reporting rate of tuberculosis. Only 1.6% of the Hong Kong versus 2.1% of the Japanese mothers reported having such a history. Yet it is known that the real rate should be much higher in Hong Kong since tuberculosis is still a common infectious disease in that community, with 137.4 new cases/100,000 population reported and a mortality rate of 8.4/100,000 (12) registered in 1983. The comparable incidence and mortality rates for Japan in 1985 were 48.4/100,000 and 3.9/100,000.

The Hong Kong subjects also reported more respiratory illnesses per person than did the Japanese subjects. These differences were especially notable among the children where the group mean values showed the Hong Kong children to be more than 2.9 times higher than those of the Japanese children ( $t$  test,  $p$  value = 0.001). No differences were observed in the frequencies of these illnesses by sex of the child.

Although the Hong Kong children were on average 8.5 months older than the Japanese children, we did not feel that this slight age difference could account for the large differences observed in the

Hong Kong children's higher reported frequencies of respiratory illnesses. In addition, the children in both populations have been immunized with the generally recommended schedule of diphtheria, pertussis, polio, BCG, etc. vaccines, so these differences were not due to immunization rates.

For both populations, however, there was a highly significant correlation between the frequency of respiratory illnesses of each mother and her child. Mothers who reported one or more illnesses for themselves were about twice as likely to report a similar number for their children.

For the Hong Kong mothers, a significant relationship was detected with increasing exposure to dust/smoke or gas/fumes in the workplace. The occurrence of respiratory illnesses seemed to be related to occupational exposures to such pollutants in 34% of those ever exposed to dust/smoke, and 46% of those ever exposed to gas/fumes. For the Hong Kong population as a whole, the attributable risk percentage was 10.0% for the former and 8.8% for the latter. However, analysis of the data by whether the mother was currently employed or not did not show any significant differences in the reported frequencies of respiratory illnesses for herself or her child.

The consistent tendency for Hong Kong subjects to have higher prevalence rates of respiratory illnesses than their Japanese counterparts is difficult to explain. Although, as shown above, some relationship was found with previous occupational exposure to dust or fumes in the workplace, the percentages of mothers currently working was not statistically different in the 2 groups.

The role of indoor air pollution in the home from passive smoking or heating/cooking activities has been investigated. Japanese fathers were about twice as likely to be smokers than were Hong Kong fathers. Moreover, in another report on the Hong Kong mothers (13), no association was found between the prevalence of chronic cough or sputum and the smoking patterns of their husbands. The etiologic role of cooking activities is also doubtful, as the proportion of kitchens with mechanical ventilation such as fans or cooking hoods was not different in Tokyo and Hong Kong. Previous case-control studies on the role of cooking fuels in lung cancer risk among females in Hong Kong (14) and Japan (15) did not find an association between fuel type (i.e., kerosene, liquid petroleum gas, charcoal, and wood/grass) and lung cancer risk.

Among the variables compared, Hong Kong families tended to be significantly larger, averaging 5.31 persons versus 4.54 for Japanese households. Among Hong Kong mothers, some association was found between larger household size and the frequency of respiratory illnesses, but such was not the case for household density. Moreover, larger household size was not associated with more respiratory illnesses among the Japanese mothers. Although both household size and density are related with socioeconomic status, the lack of an association with household density in Hong Kong would seem to indicate that these variables were not simply surrogate measures of household income. This is because, with the extremely expensive rental situation in Hong Kong, higher density living is directly associated with less income, whereas household size may reflect the persistence of an extended family system and, traditionally, according to the Confucian ethos, 3-generation families are desirable.

Several possibilities may help explain the patterns of respiratory illnesses in both populations. Recall bias may play a role as there was an increasing tendency for mothers reporting one or more respiratory illnesses for themselves to report the same for their children. This tendency was found in both the Japanese and the Hong Kong mothers, so it would not explain their highly different prevalence rates of respiratory illnesses. The principle of recall bias may have operated also on the finding that occupational exposures were related to respiratory illnesses among the Hong Kong mothers, since those with such illnesses may have been more likely to recall such past exposures than those without such problems. However, occupational exposures to such pollutants could only account for 9 to 10% of the respiratory illnesses in the Hong Kong mothers.

The role of cross infection, i.e., mother to child or other household members to mother or child, seems suggested by: (1) the direct association between household size and frequency of respiratory illnesses in the Hong Kong mothers, (2) the correlation between multiple respiratory illnesses within each mother-child pair in both populations, and (3) that Hong Kong families were significantly larger than Japanese families. However, no such association was found with household density, which would seem a more direct measurement of the potential for cross infection since the chances of spreading infectious respiratory diseases should be correlated with higher household densities. It appears that other not yet identified

environmental factors are needed to explain these results.

The findings of this study, showing mothers and especially children in Hong Kong to have larger numbers of sick subjects and to have more illnesses per subject than their Japanese counterparts, are consistent with the findings of other surveys in both areas. Questions added to an international survey in 1986 on passive smoking and urinary cotinine levels sponsored by the International Agency for Research on Cancer indicated that women in Hong Kong were about 10 times more likely to report symptoms of chronic cough or phlegm than were women in Sendai, Japan. A population survey of respiratory illnesses in Japan in 1983 (T. Mori, personal communication) indicated that the reported age-adjusted rates of such illness for non-smoking women in Japan were similar to those reported among the Japanese mothers in this survey. Thus, we feel that the reported differences in the frequencies of respiratory illnesses in Hong Kong and Japan are not artifactual.

These results agree with the contrasting female lung cancer incidence rates in the 2 areas. The epidemiologic data showed that chronic bronchitis was associated with increased risk for lung cancer in females (1). Moreover, the multistage model of carcinogenesis makes this association biologically plausible since these symptoms result from and result in a chronic irritation effect on the respiratory tract, making it more susceptible to the action of carcinogenic initiators or promoters. Previous occupational exposure to dust or fumes was associated with respiratory illnesses in the Hong Kong mother, and frequencies of such illnesses in the mother were directly related to those in her child. Although this could account for a portion of the respiratory illnesses, more investigation is needed to find other etiologic agents in the Hong Kong environment to account for the higher frequency of respiratory health problems. A recent time-trend analysis by Barker and Osmond (16) in England and Wales showing that respiratory diseases in childhood led to higher mortality rates from chronic bronchitis and emphysema later in adult life, ominously suggests that the high rates of childhood respiratory illnesses found in the Hong Kong population today portends to excess mortality from respiratory diseases in the future when these children reach 40+ yr of age.

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**ABSTRACT:** Factors contributing to differences in the prevalences of respiratory symptoms and diseases among ethnic groups were studied in primary schoolchildren living in 20 innercity areas of England in 1983. The raised prevalences of respiratory symptoms in these groups were compared with results from a national representative sample of children studied in 1982. Data on age, sex, respiratory illness, and social and environmental variables were obtained by questionnaire for 4815 children living in innercities. The children were classified as white, Afro-Caribbean, Urdu, Gujarati, Punjabi, other Asian, or "other." Significant differences in the prevalence of respiratory conditions were found among the ethnic groups after allowance was made for the effects of interfering variables. Except for asthma all conditions were most prevalent in Afro-Caribbeans and whites. In these two ethnic groups respiratory illness was significantly associated with belonging to a one parent family and the combined use of gas cookers and paraffin heaters at home.

Respiratory illness was found to vary in prevalence among ethnic groups but may be perceived differently by different groups. Further studies, measuring lung function, are necessary.

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Thus any benefit of anticoagulants is likely to be modest, and a large randomised trial would be required to detect it reliably. Of course, any modest benefit would be offset by the complexity, side effects, and cost of the treatment; in any case, a rather small population of patients with stroke are eligible for such treatment.<sup>12</sup> On the other hand, our negative results, based on a non-randomised comparison and with fairly wide confidence intervals, are unlikely to convince doctors who are already using long term anticoagulant treatment despite the lack of good data to support their opinion. To resolve this dilemma we are planning a three year randomised trial of 1200 patients to compare treatment with anticoagulants, aspirin, and placebo.

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# Respiratory illness and home environment of ethnic groups

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## Abstract

Factors contributing to differences in the prevalences of respiratory symptoms and diseases among ethnic groups were studied in primary schoolchildren living in 20 inner city areas of England in 1983. The raised prevalences of respiratory symptoms in these groups were compared with results from a national representative sample of children studied in 1982. Data on age, sex, respiratory illness, and social and environmental variables were obtained by questionnaire for 4815 children living in inner cities. The children were classified as white, Afro-Caribbean, Urdu, Gujarati, Punjabi, other Asian, or "other." Significant differences in the prevalence of respiratory conditions were found among the ethnic groups after allowance was made for the effects of interfering variables. Except for asthma all conditions were most prevalent in Afro-Caribbeans and whites. In these two ethnic groups respiratory illness was significantly associated with belonging to a one parent family and the combined use of gas cookers and paraffin heaters at home.

Respiratory illness was found to vary in prevalence among ethnic groups but may be perceived differently by different groups. Further studies, measuring lung function, are necessary.

## Introduction

The health of ethnic minority groups in the United Kingdom has been the subject of considerable discussion and concern during the past two decades. Inherited disorders such as sickle cell anaemia and illnesses such as rickets have been highlighted.<sup>1,2</sup> Respiratory health has not been studied thoroughly, though a higher prevalence of respiratory illness has been reported in West Indians<sup>3</sup> and respiratory illness in infants was reported to be more common among Bengalis than the indigenous population of an inner city area.<sup>4</sup> The cause of these differences has not been studied in detail, although poor social circumstances are probably a factor in some ethnic groups. As respiratory disease in childhood has been linked with susceptibility to respiratory disease in later life<sup>5</sup> it is important to investigate the causes of variation in respiratory health between children of different ethnic groups to identify preventive measures.

This study of primary schoolchildren investigated the prevalence of respiratory illness in ethnic groups in inner city areas and factors that contribute to differences in prevalence among the ethnic groups and between the groups from inner cities and a national sample of children.

## Subjects and methods

In 1983 data on respiratory symptoms and diseases were collected in the national study of health and growth, a surveillance study of primary schoolchildren that included white, Afro-Caribbean, Indian, and Pakistani children from inner city areas,<sup>6</sup> most of whom had spent most of their lives in Britain. Twenty wards in England with a high percentage of children of Afro-Caribbean and Indo-Pakistani ethnic origin and children living in inner city areas with a high level of overcrowding, unemployment, or lack of exclusive use of amenities had been selected, and about 350 children aged 5-11 from one or two schools close to the geographical centre of each ward had been studied. In 1983 the study investigated ethnic minorities for the first time. Several factors were studied in connection with respiratory disease but smoking was not one of them. To assess further the size of the

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problem of respiratory disease in inner cities we included in our study data on white primary schoolchildren from the 1982 national study of health and growth; these children had a similar social class distribution to other representative national samples.<sup>7</sup> The methods of collecting data closely resembled those used in 1983, although data on "colds going to the chest" were not collected.

In 1983 data on respiratory illness in the children were collected from a questionnaire completed by a parent of each child. The questionnaire was available in English, English and Urdu, English and Gujarati, and English and Punjabi. It asked whether the child usually had a cough first thing in the morning, cough during the day or night, or colds that "went to the chest"; whether the child's chest ever sounded wheezy or whistling; and how many attacks of bronchitis or asthma had been experienced during the past 12 months. Other questions were asked about the number of children at home, mother's occupation, mother's educational attainment, uptake of free school meals, and types of fuel used for cooking and heating at home. Ethnic group was ascertained from assessments made by fieldworkers and the main language spoken at home.

Prevalences of respiratory conditions were compared with the  $\chi^2$  test and by logistic regression using the computer program GLIM.<sup>8</sup> As the respiratory conditions were interrelated an overall measure of respiratory illness (the presence of one or more respiratory conditions) was also used. Two main groups of regression analyses were carried out on the 1983 sample. Firstly, ethnic groups were compared allowing for age, sex, area of residence, mother's educational attainment, and number of children at home. Area of residence was included as the ethnic minority groups came mainly from the areas specifically selected to include those groups, and the prevalence of respiratory illness in children might be related to environmental factors not otherwise considered in our analysis. Mother's educational attainment, classified into three groups (no formal education or primary, only, primary, and secondary, college or university), was used instead of social class to indicate social circumstances. Secondly, for whites and Afro-Caribbeans the additional effects of living in a one parent family and living in a home with a gas cooker or paraffin heaters were studied. Gas cookers and paraffin heaters are indoor sources of air pollution, particularly nitrogen dioxide.<sup>9</sup> Homes were placed in one of three groups according to the expected level of nitrogen dioxide: homes with an electric cooker and no paraffin heaters, homes with a gas cooker and no paraffin heaters, and homes with both a gas cooker and paraffin heaters. Homes with paraffin heaters alone or with coal fires, another important source of indoor air pollution, were excluded because their numbers were too small (Living in a one parent family and the effects of indoor air pollution could not be studied in the Asian group, because the question on one parent families had been incorrectly translated and too few homes had electric cookers or paraffin heaters, less than 15 and less than seven, respectively in each Asian group).

Additional regression analyses were carried out to compare respiratory symptoms between white children studied in 1982 and 1983. The effects of age, sex, father's social class, living in a one parent family, mother's education, and number of children at home were allowed for in this comparison.

## Results

Data on 4813 children (67.8% of the 7103 children in the 1983 sample) were obtained. Absence of data on the six respiratory conditions, mother's education, or type of fuel used for cooking excluded a further 1906. The response rate varied among ethnic groups, with Afro-Caribbeans having a response rate of 58%, Urduis 69%, "other ethnic groups" 56%, and each remaining group more than 70%. The 2105 white children from the 1983 sample were compared with 4849 white children from the 1982 sample (70.7% of the 6862 studied). These samples were similar in their age and sex distributions.

Tables I and II show the unadjusted prevalences of respiratory symptoms and diseases in boys and girls studied in 1983 by ethnic group. The prevalence of all conditions except cough in the morning in both sexes and asthma in boys varied significantly among ethnic groups ( $p < 0.01$ ). In both sexes cough during the day or night and colds going to the chest tended to be most prevalent in whites and Afro-Caribbeans. Bronchitis was most prevalent in whites, and wheezing in whites and Afro-Caribbeans. For the other respiratory conditions, differences in prevalence among ethnic groups were inconsistent between the sexes. The overall measure of respiratory illness, the presence of one or more respiratory conditions, was found most commonly in Afro-Caribbeans and least commonly in Gujaratis. The prevalences in whites were high not only compared with those in the other ethnic groups but also compared with those in the 1982 sample.

Each respiratory condition was analysed separately for the effects of age, sex, mother's education, number of children in family, and area of residence. The prevalence of all conditions except asthma declined significantly with age ( $p < 0.05$ ) and tended to be higher in boys than girls. The prevalences showed some association with mother's education, tending to be higher among children of mothers with no formal education or only elementary education and lowest among children whose mothers had been to college or university, but significantly so only for coughs ( $p < 0.05$ ). The presence of four or more children in the family was associated with high prevalences of coughs ( $p < 0.05$ ), but the other conditions were reported most commonly for single children ( $p < 0.05$ ). Areas of residence was related to the prevalence of cough in the morning, wheezing, and bronchitis ( $p < 0.05$ ). The first order interactions among these independent variables on

TABLE I.—Unadjusted percentage number of respiratory conditions by ethnic group among boys.

	White		Afro-Caribbean (n=261)	Urdu (n=157)	Gujarati (n=221)	Punjabi (n=451)	Other Asian (n=110)	Other (n=140)	Total 1983 (n=2429)
	1982 (n=2087)	1983 (n=1089)							
Cough in the morning	3.5 (48)	7.7 (64)*	8.8 (33)	9.6 (15)	3.6 (8)	8 (38)	4.7 (5)	3.6 (5)	7.3 (18)
Cough during day or night	7.3 (103)	15.6 (120)*	18.4 (48)	8.9 (16)	8.1 (18)	10.0 (45)	8.7 (8)	9.3 (13)	13.1 (31)*
Cough during day or night + wheezing	11.1 (127)	15.5 (109)*	14.9 (39)	10.2 (16)	5.9 (13)	10.0 (45)	7.7 (8)	10.0 (14)	12.7 (30)*
"Chest going to chest"	3.7 (93)	24.2 (372)*	33.3 (87)	19.2 (31)	17.2 (38)	21.8 (37)	25.5 (28)	28.4 (37)	28.6 (40)*
Bronchitis	3.7 (93)	7.6 (83)*	3.4 (9)	1.3 (2)	1.3 (2)	1.8 (4)	2.3 (5)	3.6 (4)	3.7 (9)
Asthma	3.0 (75)	3.5 (38)	1.5 (4)	6.4 (10)	6.4 (10)	2.3 (5)	4.7 (21)	3.6 (4)	5.7 (8)
One or more respiratory conditions	40.9 (445)	41.8 (109)	28.0 (44)	23.1 (31)	23.1 (31)	28.4 (38)	30.0 (33)	33.6 (42)	35.3 (87)*

\*White, 1982 v 1983,  $\chi^2$  test, df=1;  $p < 0.001$

†All ethnic groups, 1983,  $\chi^2$  test, df=6;  $p < 0.001$

TABLE II.—Unadjusted percentage number of respiratory conditions by ethnic group among girls.

	White		Afro-Caribbean (n=284)	Urdu (n=186)	Gujarati (n=220)	Punjabi (n=436)	Other Asian (n=108)	Total	
	1982 (n=3352)	1983 (n=1016)						1982 (n=136)	1983 (n=2386)
Cough in morning	3.8 (90)	7.3 (74)**	9.9 (28)	4.8 (18)	7.3 (16)	5.5 (24)	10.2 (11)	5.1 (8)	7.1 (10)*
Cough during day or night	8.1 (190)	15.2 (154)**	14.5 (42)	9.6 (18)	10.5 (23)	8.5 (37)	13.0 (14)	6.1 (10)	12.5 (22)*
Cough during day or night and wheezing	8.1 (190)	11.6 (118)*	12.0 (34)	12.0 (20)	5.5 (12)	6.7 (29)	5.6 (6)	6.4 (10)	9.6 (13)*
"Chest going to chest"	32.7 (332)	32.7 (332)	30.6 (87)	30.6 (47)	30.6 (47)	15.1 (25)	12.7 (28)	14.7 (16)	24.9 (36)*
Bronchitis	4.2 (51)	5.6 (55)**	4.2 (12)	0.6 (1)	0.6 (1)	0.3 (1)	0.0 (0)	3.4 (6)	1.9 (46)**
Asthma	1.9 (44)	1.1 (11)	2.1 (6)	3.6 (16)	3.6 (16)	0.5 (1)	0.5 (1)	28.9 (29)	31.7 (35)*
One or more respiratory conditions	38.2 (388)	39.1 (111)	24.7 (41)	19.1 (42)	19.1 (42)	23.2 (10)	23.2 (10)	28.9 (29)	31.7 (35)*

\*White, 1982 v 1983,  $\chi^2$  test, df=1;  $p < 0.01$ , \*\* $p < 0.001$

†All ethnic groups, 1983,  $\chi^2$  test, df=6;  $p < 0.01$ , \*\* $p < 0.001$

each respiratory symptom were not significant. Significant differences in the prevalence of all conditions were found among the ethnic groups ( $p < 0.05$ ), after allowance was made for the effects of the independent variables. These results were similar to those for the unadjusted prevalences and are illustrated in table III adjusted to boys aged 8 with a mother with secondary school education and with one sibling.

The second set of regression analyses, conducted in 2022 whites and 530 Afro-Caribbeans, studied additionally the effects of belonging to a one parent family and of living in a home in which gas cookers or paraffin heaters were used. Table IV gives the relative risk of respiratory conditions associated with mother's education, number of children in the family, belonging to a one parent family, and use of gas cookers and paraffin heaters. Results for asthma and bronchitis showed no significant relation to any of these factors and are not shown. High risks of all the conditions shown in table IV were associated with one parent families compared with two parent families ( $p < 0.05$ ). The risk of respiratory illness increased when two or more sources of nitrogen dioxide (a gas cooker and paraffin heaters) were present in the home. The association between gas cookers alone and respiratory illness approached significance for cough in the morning and wheeze ( $p < 0.1$ ). The association between respiratory illness and the combined use of a gas cooker and paraffin heaters was significant for colds going to the chest and the presence of one or more respiratory conditions ( $p < 0.05$ ). For a subset of 2164 whites and Afro-Caribbeans regression analysis of each respiratory condition was conducted to include father's social class and uptake of free school meals. The effects on respiratory illness of one parent families and the combined use of gas cookers and paraffin heaters remained significant for colds going to the chest ( $p < 0.05$ ) and borderline for the overall measure ( $p = 0.052$ ).

To assess further the problem of respiratory illness in inner cities the prevalence of respiratory conditions in the 1983 sample of white children was compared with the prevalence in the 1982 national representative sample after allowance had been made for the effects of interfering variables. The prevalences of cough in the morning, cough during the day or night, wheezing, and bronchitis were significantly higher in 1983 than 1982 ( $p < 0.05$ ).

## Discussion

In our study Afro-Caribbeans and white people living in inner cities had higher prevalences of several conditions compared with Asians. In a national cohort of children the prevalence of wheezing was significantly higher in children with West Indian and British parents than those with Asian parents ( $p < 0.01$ ), but the prevalence

of asthma and bronchitis did not differ among ethnic groups.<sup>12</sup> West Indian and Bengali infants have been reported to attend accident and emergency departments because of respiratory disease more commonly than white children, but this may partly reflect a different pattern of use of health services by ethnic groups. Smith found asthma and wheezing in 5-6 year olds to be more prevalent in West Indians born in England than in Asians born in England or abroad.<sup>13</sup> It is unclear, however, which groups of Asians were being studied. In our study the prevalence of asthma differed among groups of Asians.

The differing results of studies may be explained partly by differences in methodology and partly by biases in the results. Three main biases should be considered. Firstly, certain ethnic groups such as Punjabis are not homogeneous, and subgroups would be expected to differ in health. The distribution of these subgroups varies in England, and a study in one area is likely to contain only one subgroup. Each ethnic group in our study lived in several areas of England, so our results cover a range of children within each group. Secondly, respiratory illness may well be perceived differently by each ethnic group, and these differences may not have been dealt with simply by translating the questionnaire. Although studies of the incidence and prevalence of respiratory disease indicate the burden of respiratory disease experienced by some groups, objective measures of respiratory illness, such as lung function, would contribute further to the study of respiratory illness in ethnic groups. Thirdly, in this study response rates varied among ethnic groups even though non-responders were followed up by health visitors and the questionnaire was available in three languages. Inclusion of non-responders known to have respiratory illness, however, made no difference to our results. The relation of respiratory illness to factors such as age was similar to previous findings, which gives some credence to our results.

A raised prevalence of respiratory illness might be expected in large families<sup>14</sup> and when the mother's educational level is low, this being associated with poor social class,<sup>15</sup> but such was not the case in this study. Single children had significantly more colds going to the chest and more wheezing ( $p < 0.05$ ) than children with three or more siblings. A mother with only one child to care for may be more aware of that child developing respiratory illness than mothers with larger

TABLE III—Mean prevalence, expressed as percentage and number (1) of respiratory conditions adjusted to boys aged 8 with mother educated up to secondary school and two children in family. Figures in each group are for the 1983 sample

	White (n=2105)	Afro-Caribbean (n=545)	Urdu (n=323)	Gujarati (n=44)	Punjabi (n=887)	Other Asian (n=218)	Other (n=296)	Total (n=4815)
Cough in morning	4.4 (158)	5.9 (51)	3.2 (23)	2.7 (24)	2.6 (62)	3.7 (16)	2.5 (13)	5.5 (347)**
Cough during day or night	14.4 (324)	15.8 (95)	6.9 (30)	7.3 (41)	6.3 (82)	8.3 (23)	6.8 (21)	10.4 (616)**
Wheezing	11.7 (267)	10.8 (73)	8.7 (36)	5.3 (25)	5.7 (78)	4.8 (14)	7.3 (24)	8.8 (537)**
Colds going to chest†	36.7 (704)	34.4 (174)	20.8 (56)	17.1 (66)	18.7 (161)	26.9 (51)	28.3 (72)	24.3 (1284)**
Bronchitis	11.6 (138)	4.6 (21)	1.9 (3)	2.6 (6)	6.7 (30)	5.1 (6)	6.0 (9)	4.4 (213)**
Asthma	3.1 (49)	2.2 (10)	7.0 (16)	1.5 (6)	5.0 (32)	4.9 (9)	6.0 (14)	3.4 (136)**
One or more respiratory conditions	46.1 (833)	46.1 (220)	32.8 (85)	25.7 (93)	28.7 (229)	34.6 (62)	37.5 (92)	35.6 (1614)**

\* $p < 0.05$ , \*\* $p < 0.001$  ( $\chi^2$  test); df=6: After allowing for effects of age, sex, mother's educational attainment, number of children in family, and area of residence

TABLE IV—Relative risk\* (95% confidence intervals) of respiratory conditions in Afro-Caribbean and white children (1983 data, n=2552) associated with characteristics of family and home

	No of children	Cough in morning	Cough during day or night	Wheezing	Colds going to chest†	One or more respiratory conditions
Mother's education						
No formal education or elementary	196	2.15† (1.4 to 3.28)	1.42† (1.04 to 1.89)	1.33 (0.95 to 1.83)	1.11 (0.92 to 1.31)	1.17 (1.0 to 1.33)
College or university	366	0.81 (0.5 to 1.31)	0.67 (0.47 to 0.93)	1.21 (0.91 to 1.53)	0.88 (0.75 to 1.04)	0.88 (0.75 to 1.00)
No of children in family						
2	902	1.54 (0.86 to 2.73)	1.05 (0.75 to 1.46)	0.74 (0.52 to 1.02)	0.84 (0.68 to 0.99)	0.84 (0.70 to 0.99)
3	699	1.82 (1.0 to 3.23)	1.22 (0.87 to 1.68)	0.89 (0.63 to 1.23)	0.85 (0.69 to 1.02)	0.90 (0.76 to 1.06)
≥4	668	1.75 (0.97 to 3.13)	1.07 (0.75 to 1.49)	0.64 (0.45 to 0.93)	0.70† (0.56 to 0.86)	0.77† (0.63 to 0.92)
One parent family	805	1.48† (1.07 to 2.03)	1.49† (1.22 to 1.8)	1.27† (1.02 to 1.56)	1.10† (1.04 to 1.28)	1.18† (1.06 to 1.28)
Cooking and heating fuels						
Gas cookers, no paraffin heaters	1964	1.48 (0.97 to 2.24)	0.93 (0.73 to 1.19)	1.27 (0.98 to 1.64)	1.10 (0.97 to 1.24)	1.06 (0.94 to 1.17)
Gas cookers, paraffin heaters	83	1.85 (0.79 to 4.25)	1.14 (0.64 to 1.90)	1.64 (0.94 to 2.83)	1.40† (1.08 to 1.71)	1.35† (1.09 to 1.59)

\*Relative to risk in white boys aged 8 with mother educated up to secondary school, one child in family, two parent family, and no gas or paraffin fuels used in the home

†Difference from relative risk of 1.0,  $p < 0.05$



families to look after. A low educational level of the mother was associated only with a high prevalence of cough ( $p < 0.05$ ). It may be inappropriate to compare educational background of ethnic groups, particularly those educated abroad, as educational categories may not be directly comparable.

Two other factors previously associated with respiratory illness in children—namely, belonging to a one parent family<sup>11</sup> and exposure to indoor air pollution from gas cookers and paraffin heaters<sup>12,13</sup>—could be studied only in Afro-Caribbeans and whites. Belonging to a one parent family is likely to measure poor social circumstances, but a single parent may be more aware of a child developing respiratory illness. The association of respiratory illness with the combined use of gas cookers and paraffin heaters might reflect poor social circumstances as well as high concentrations of nitrogen dioxide indoors, which may sometimes exceed the European Community's directive for outdoor concentrations of nitrogen dioxide.<sup>14</sup> Parental smoking habit was not analysed, though smoking has been reported to be more common among Afro-Caribbeans and whites than Asians.<sup>15</sup>

This survey highlights the problem of respiratory disease in children living in inner cities. Such disease was significantly more prevalent in whites compared with all groups in the national sample and varied considerably among ethnic groups. Strong evidence suggests that childhood respiratory illness leads to poor respiratory health in adulthood.<sup>16</sup> We intend to study the variation in respiratory illness among ethnic groups further.

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## SHORT REPORTS

### Is surgical closure of the back lesion in open neural tube defects necessary?

Early closure of the lesion is believed to be central to the management of open neural tube defects. Non-closure of the defect, however, does not necessarily increase morbidity to mortality.<sup>1-3</sup> Since 1978 open neural tube defects in patients with a poor prognosis have not been closed at our unit, but the patients have received full medical and nursing care, including antibiotics and shunts for hydrocephalus when necessary. We compared these patients with an earlier group who had received early closure as an urgent treatment.

#### Patients, methods, and results

We reviewed patients with open neural tube defects above L2 or hydrocephalus at birth, or both. Altogether 109 had been born between 1964 and 1971 and 105 born between 1978 and 1985. Treatment policies differed only in that children born between 1964 and 1971 had received early closure of the defect whereas for children born between 1978 and 1985 closure had not been performed or had been deferred until they were at least 3 months old. Data were analysed with the statistical package for the social sciences life tables and the Lee-Desu statistic. Patients who died before they developed a complication were included as "censored" data. Mortality and the incidence of hydrocephalus, insertion of a shunt, ventriculitis, and ventriculitis before insertion of a shunt were compared by relating the difference at any time to the standard error of the difference expressed as a standardised normal z statistic.

No significant difference in the sex ratio, number of children born with hydrocephalus, or number of children with a neurological level above L2 was found between the two groups. The table shows that non-closure resulted in a significantly lower incidence ( $p < 0.001$ ) of hydrocephalus, insertion of a shunt, ventriculitis, and ventriculitis before insertion of a shunt during the first five months of life but did not affect mortality throughout the first year. After the first year there was no significant difference in any of the complications between the groups.

Hydrocephalus correlated with ventriculitis ( $p < 0.001$ ) during the first year, among those whose wound was not closed 37 of the 72 patients with hydrocephalus developed ventriculitis compared with six of the 37 without hydro-

Cumulative survival and proportions SE of babies with open neural tube defects without the complications specified at one, three, six, and 12 months

	Months from birth			
	1	3	6	12
Survival				
Early closure	0.86:0.03	0.78:0.04	0.65:0.05	0.51:0.05
Non-closure	0.81:0.04	0.73:0.04	0.64:0.05	0.50:0.05
Without hydrocephalus				
Early closure	0.40:0.07*	0.12:0.05*	0.08:0.05*	0.08:0.05
Non-closure	0.83:0.05	0.46:0.07	0.25:0.06	0.10:0.05
Without a shunt				
Early closure	0.64:0.05*	0.18:0.05*	0.13:0.04*	0.11:0.04
Non-closure	0.76:0.05	0.51:0.05	0.29:0.05	0.13:0.04
Without ventriculitis				
Early closure	0.84:0.04*	0.64:0.05*	0.58:0.05	0.48:0.06
Non-closure	0.94:0.03	0.78:0.04	0.69:0.05	0.48:0.06
Without ventriculitis before insertion of a shunt				
Early closure	0.72:0.05*	0.69:0.06	0.66:0.06	0.66:0.06
Non-closure	0.90:0.06	0.85:0.07	0.75:0.09	0.75:0.09

\*Significance of difference between groups  $p < 0.001$ .

cephalus, and similar results were found for the babies who received early closure.

#### Comment

We are aware of the caution necessary in analysing historical data. Nevertheless, the finding that mortality did not increase when the neural tube lesion was not closed implies, contrary to previous belief, that early closure as an urgent procedure is not essential for an optimal prognosis. Similarly, the incidence of ventriculitis and, more importantly, of ventriculitis before shunting was reduced during the first three months by non-closure of the defect, suggesting that early closure may not be necessary to reduce the risk of ascending infection.

The incidence of both hydrocephalus and insertion of a shunt was

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Goren, A.I., Hellmann, S. "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel" Environmental Research 45: 28-37, 1988.

SUMMARY: Second and fifth grade schoolchildren living in two communities with different levels of air pollution were studied. The parents of these children filled out ATS-NHLI health questionnaires. The prevalence of reported respiratory symptoms and pulmonary diseases was found to be significantly higher among children growing up in the polluted community (Ashdod) as compared with the low-pollution area (Hadera). Logistic models fitted for the respiratory conditions which differed significantly between both areas of residence also included background variables that could be responsible for these differences. Relative risk values, which we calculated from the logistic models, were in the range of 1.47 for cough without cold to 2.66 for asthma for children from Ashdod, as compared with 1.00 children from Hadera.

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## Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel<sup>1</sup>

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Second and fifth grade schoolchildren living in two communities with different levels of air pollution were studied. The parents of these children filled out ATS-NHLI health questionnaires. The prevalence of reported respiratory symptoms and pulmonary diseases was found to be significantly higher among children growing up in the polluted community (Ashdod) as compared with the low-pollution area (Hadera). Logistic models fitted for the respiratory conditions which differed significantly between both areas of residence also included background variables that could be responsible for these differences. Relative risk values, which were calculated from the logistic models, were in the range of 1.47 for cough without cold to 2.66 for asthma for children from Ashdod, as compared with 1.00 for children from Hadera. © 1988 Academic Press, Inc.

### INTRODUCTION

It is well known that high air pollution concentrations may influence morbidity and mortality from respiratory conditions. However, the health impact of long-term exposure to low concentrations of air pollutants is not fully known. Many surveys have been carried out during the last decades in an effort to detect possible health effects resulting from long-term exposure to low concentrations of air pollution. In these surveys, which were mainly carried out among adults, it was demonstrated that factors such as smoking and occupational exposure are correlated with the incidence and prevalence of respiratory conditions (Colley and Holland, 1967; Colley *et al.*, 1973; Goldsmith and Friberg, 1977; Holland *et al.*, 1969a; Irvine *et al.*, 1980). Since the effects of air pollution on the respiratory tract are relatively low as compared with those of smoking, controlling for such factors in the analysis is crucial.

Many surveys have recently been conducted among young children who are not occupationally exposed and do not smoke (Biersteker and Leeuwen, 1970; Colley and Brasser, 1980; Colley and Reid, 1970; Ferris, 1978a; Goren and Goldsmith, 1986; Holma *et al.*, 1979; Irvine *et al.*, 1980; Lunn *et al.*, 1967; Melia *et al.*, 1981; Mostardi *et al.*, 1981a; Mostardi *et al.*, 1981b; Toyama, 1964).

However, many variables other than smoking and occupational exposure may affect the respiratory system in the same direction as air pollution and should therefore be taken into account in the analysis. Such variables are socioeconomic

<sup>1</sup> This survey was supported by a grant from the Israel Ministry of Health.

status (Colley and Reid, 1970; Goren and Goldsmith, 1986; Holland *et al.*, 1969a, b; Melia *et al.*, 1981; Peat *et al.*, 1980), crowding index (Holma *et al.*, 1979; Leeder *et al.*, 1976; Lunn *et al.*, 1967; Peat *et al.*, 1980), type of fuel used in household (Hasselblad *et al.*, 1981), smoking habits of adults at home (Bland *et al.*, 1978; Cameron *et al.*, 1969; Colley, 1974; Fergusson *et al.*, 1980; Fergusson *et al.*, 1981; Goren and Goldsmith, 1986; Hasselblad *et al.*, 1981; Lebowitz and Burrows, 1976; Leeder *et al.*, 1976; Schilling *et al.*, 1977; Tager *et al.*, 1979; Vedal *et al.*, 1984; Ware *et al.*, 1984), and respiratory diseases among family members of the observed children (Colley, 1974; Goren and Goldsmith, 1986; Higgins and Keller, 1975; Leeder *et al.*, 1976; Schilling *et al.*, 1977; Tager *et al.*, 1978). This work was carried out in order to compare the health status of children growing up in a polluted area with that of children in a clean one, taking into account all the above-mentioned factors. It was assumed that children growing up in a region with elevated sulfur dioxide concentrations suffer from more respiratory symptoms and diseases as compared with children growing up in a clean area.

#### MATERIALS AND METHODS

This survey was carried out among schoolchildren from two communities located along the Israeli coast 80 km from each other, but differentially exposed to air pollution. One group lives in Ashdod (Fig. 1), which is an industrialized town, mainly polluted by an 1100-MW oil-fired power station, refineries, and a complex industrial zone (which includes a herbicide factory and acrylic fiber and lead-melting plants). The population of this area numbers about 65,000 (the country of origin of their fathers: 32%, Europe-America: 49%, North Africa: 14%, Asia: and 5%, Israel). The second group lives in Hadera, which was an unpolluted area in 1980 (when this survey was carried out). These baseline health data in Hadera were gathered in the framework of a prospective epidemiological monitoring program carried out in this area since a new 1400-MW coal-fired power plant was to begin operating there in 1982 (Toeplitz *et al.*, 1984). The population of this area numbers about 76,000 persons (the country of origin of their fathers: 39%, Europe-America: 28%, North Africa: 19%, Asia: and 14%, Israel).

**Study population.** Second and fifth grade pupils from 24 schools in Hadera and surroundings (a low-pollution area) were studied in 1980. In 1982 second and fifth grade pupils from 15 schools in Ashdod and surroundings (a polluted area) were surveyed.

**Health questionnaire.** The health questionnaire (Ferris, 1978b) used in this study is a translation into Hebrew of the ATS-NHLI (American Thoracic Society and the National Heart and Lung Institute) health questionnaire to be self-administered by the children's parents. The questionnaires were distributed in both communities between March and June by the school nurse, who also collected them after they had been filled out. From the health questionnaires the following information was obtained: respiratory symptoms and diseases of the children, socioeconomic status, type of household fuel used, smoking habits of the parents, respiratory problems in the families.

Of the 1984 questionnaires distributed in the Hadera area, 1702 were returned—a response rate of 85.8%. In Ashdod, 1826 questionnaires were distributed and 1672 were filled out—a response rate of 91.6%. In both areas, almost all the

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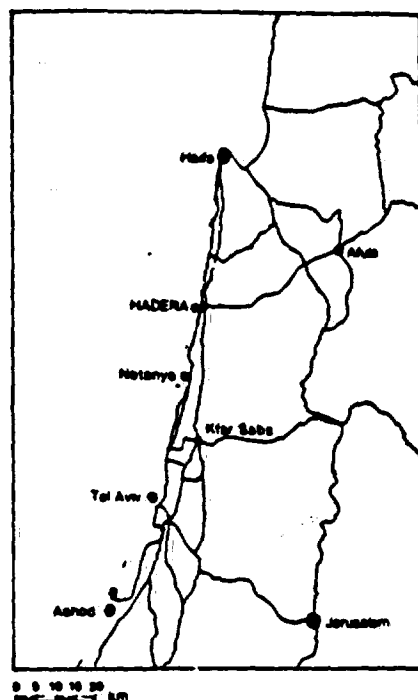


FIG. 1. Site of the two communities Hadera (nonpolluted) and Ashdod (polluted).

children of the studied cohorts living in the community for at least 5 years were examined.

**Air pollution measurements.** Air pollution measurements are carried out in the Hadera area by the local municipal authorities and in the Ashdod area by the electric company. The monitoring stations in the Hadera area (low pollution) are fully automatic and measure  $\text{SO}_2$ ,  $\text{NO}$ ,  $\text{NO}_2$ ,  $\text{NO}_x$ , total hydrocarbons,  $\text{O}_3$ ,  $\text{CO}$ , TSP, and various atmospheric parameters (such as temperature and humidity).  $\text{SO}_2$  is measured by means of a flame photometric instrument, and  $\text{NO}_x$  by a chemiluminescent apparatus.

The monitoring stations in the Ashdod area (polluted) are automatic and measure  $\text{SO}_2$ ,  $\text{NO}_x$ , soiling index, and meteorological parameters.  $\text{SO}_2$  is measured by means of a conductometric instrument and  $\text{NO}_x$  by a chemiluminescent apparatus.

**Analytic procedure.** Statistical analysis of the data was carried out by means of the SPSS program (Nie *et al.*, 1975). Prevalence of respiratory symptoms and diseases according to place of residence was analyzed by means of the  $\chi^2$  test for examination of independence between two variables. The possible effect of a different distribution of background variables in both areas of residence was examined by stratification.

In order to examine the combined effect of all variables in each area, a non-

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hierarchical logistic model (Dixon *et al.*, 1981) was fitted for the frequency of each respiratory symptom or disease. Those background variables which were included in the logistic regression for each population and the areas of residence were included in the logistic model fitted for the respiratory condition in the pooled data set of both populations. The equation for the predicted proportion of the respiratory condition  $E(f)$  according to the logistic regression is  $E(f) = e^f / 1 + e^f$  in which  $f$  is the frequency of the respiratory condition.  $n$  is the sample size.  $u = \alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_m x_m$  in which  $x_1, x_2, \dots, x_m$  are the background (binary) variables and  $\alpha, \beta_1, \beta_2, \dots, \beta_m$  are the coefficients.

The logistic regression estimates the coefficients of the background variables (such as father's country of origin, crowding index, type of household fuel used, smoking habits of parents, and respiratory diseases among children's fathers) in a stepwise manner.

The relative risk ( $RR$ ) to suffer from a respiratory condition in the polluted community as compared with the low-pollution community was calculated from the logistic regression as follows:  $RR = e^{\beta_1}$  where  $\beta_1$  is the coefficient of the area of residence.

### RESULTS

$SO_2$  concentrations—both monthly averages and maximal half-hourly concentrations—are much higher in Ashdod than in Hadera. The same holds for  $NO_x$  concentrations in both areas (Table 1).

The frequency of reported respiratory symptoms (Fig. 2) among schoolchildren from Ashdod, the polluted area, is higher than among children growing up in the

TABLE I  
MONTHLY AVERAGES AND MAXIMAL HALF-HOURLY CONCENTRATIONS OF SULFUR DIOXIDES ( $\mu g m^{-3}$ ) AND  $NO_x$  (ppb) IN ASHDOD (POLLUTED AREA) AND IN HADERA (LOW POLLUTED AREA) IN 1982

Month	Hadera				Ashdod			
	$SO_2$ ( $\mu g m^{-3}$ )		$NO_x$ (ppb)		$SO_2$ ( $\mu g m^{-3}$ )		$NO_x$ (ppb)	
	Monthly average	Maximal $\frac{1}{2}$ hr	Monthly average	Maximal $\frac{1}{2}$ hr	Monthly average	Maximal $\frac{1}{2}$ hr	Monthly average	Maximal $\frac{1}{2}$ hr
January	7.0	416	7.7	53	27.7	276	32.3	528
February	7.0	99	6.9	37	42.4	402	7.7*	38
March	6.5	179	8.4	76	22.7	493	13.3	43
April	6.2	146	8.2	57	40.6	670	19.8	127
May	5.2*	169	10.2*	94	45.2	836	32.3	176
June	3.1	135	8.0	95	18.1	415	7.9	69
July	2.6	68	7.3	128	10.6	309	11.3	76
August	1.0	18	6.4	60	18.1	133	11.6	97
September	4.7	140	7.5	64	21.1	417	19.3	63
October	3.4*	166	6.2*	39	28.6	451	17.6	74
November	2.1*	203	6.9*	71	33.0	295	14.8*	78
December	1.8	62	7.0	48	30.4	595	33.3*	200

\* Data availability less than 50%.

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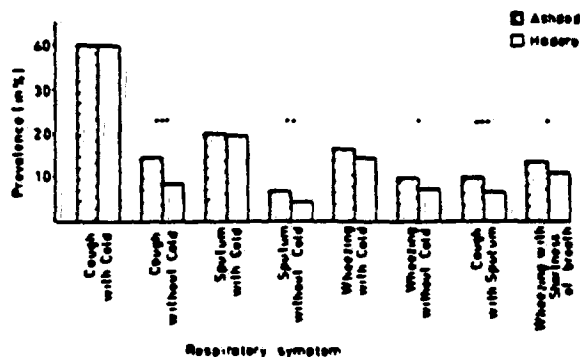


FIG. 2. Prevalence of respiratory symptoms (in %) among second and fifth grade school children from Ashdod (polluted area) and from Hadera (nonpolluted area). \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

nonpolluted area (Hadera). Cough without cold, sputum without cold, wheezing without cold, attacks of cough with sputum, and wheezing accompanied by shortness of breath are significantly more common among Ashdod children. It should be emphasized that transient respiratory symptoms, namely, cough with cold, sputum with cold, and wheezing with cold, are not significantly more common among children from the polluted area.

Figure 3 summarizes the frequency of reported respiratory diseases (in %) in second and fifth grade schoolchildren in Ashdod and Hadera. Chest illnesses that kept children from their usual activities, chest illnesses with sputum production, number of such illnesses, pneumonia, bronchitis, and asthma are significantly more prevalent among children growing up in Ashdod. On the other hand, illnesses such as measles, sinus trouble, ear infections and allergy are not significantly more common among Ashdod children. Analysis of background variables which may influence the prevalence of respiratory conditions of the children shows that children in Ashdod grow up in more crowded homes, in fewer houses

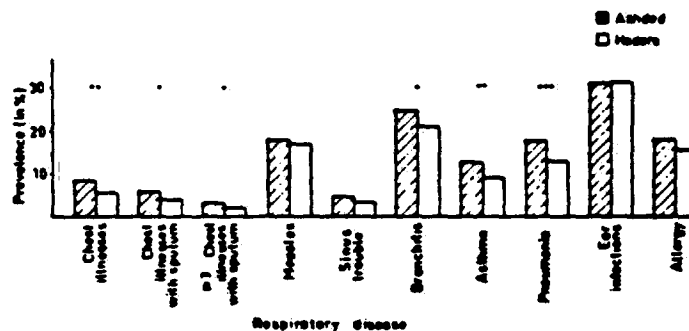


FIG. 3. Prevalence of respiratory diseases (in %) among second and fifth grade school children from Ashdod (polluted area) and from Hadera (nonpolluted area). \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .



with heat, their fathers report more respiratory problems, and their fathers are more frequently from oriental countries, as compared with children from Hadera (Table 2). The effect of these background variables on the prevalence of respiratory problems among Ashdod children was controlled for in further analytic procedures.

It could be shown, by stratification, that the different prevalence of respiratory symptoms and diseases among children from Ashdod and Hadera remains consistent (although not always statistically significant) within the subgroups of background variables. For instance, among children whose houses are heated (Table 3), the prevalence of respiratory symptoms and diseases is higher in Ashdod children than in Hadera children; the difference is statistically significant for most symptoms and diseases.

The logistic models fitted for the respiratory conditions which differed significantly between both areas of residence enabled a calculation of the relative risk to suffer from a respiratory condition in Ashdod as compared with Hadera. Most of the models fitted included the area of residence as a significant component (Table 4). All the models included some background variables, especially respiratory conditions of the fathers.

Most of the models fitted for respiratory conditions demonstrate well the interactions between the respiratory conditions and the background variables.

The relative risks calculated for respiratory conditions in Ashdod are between 1.47 for cough without cold and 2.66 for asthma, as compared with 1.00 for Hadera children.

### DISCUSSION

Our results are in accord with findings in the literature, which indicates a higher prevalence of respiratory symptoms and diseases among children growing up in polluted as compared with nonpolluted areas. The WHO collaborative study on the relationship between air pollution and respiratory diseases in chil-

TABLE 2  
FREQUENCY (IN %) OF BACKGROUND VARIABLES AMONG SECOND AND FIFTH GRADE  
SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AND HADERA (NONPOLLUTED AREA)

Background variable	Frequency in Hadera (%)	Frequency in Ashdod (%)	P value
Crowding index ( $\geq 1.5$ persons/room)	56.0 (1738)*	61.3 (1368)	0.003
No heating	12.6 (1791)	24.0 (1450)	<0.001
Father's education ( $\leq 8$ years)	29.7 (1682)	27.3 (1304)	N.S. (0.168)*
Mother smoking	21.6 (1744)	16.1 (1391)	<0.001
Respiratory diseases among fathers	8.3 (1557)	10.8 (1162)	0.034
Oriental origin of father	52.5 (1775)	48.2 (1420)	<0.001

\* Number of children in parentheses.

\*  $P > 0.05$  is considered as N.S.

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TABLE 3  
PREVALENCE (IN %) OF RESPIRATORY SYMPTOMS AND DISEASES AMONG SECOND AND FIFTH  
GRADE SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AND HADERA (NONPOLLUTED AREA)  
WITHIN THE SUBGROUP OF CHILDREN WHOSE HOUSES ARE HEATED

Respiratory symptom or disease	Prevalence in Hadera (%)	Prevalence in Ashdod (%)	P value
Cough with cold	39.9 (1536)*	40.1 (1080)	N.S.(0.957)*
Cough without cold	8.2 (1530)	14.8 (1075)	<0.001
Sputum with cold	19.1 (1485)	20.8 (1050)	N.S.(0.333)
Sputum without cold	3.9 (1481)	6.9 (1038)	0.001
Wheezing with cold	14.0 (1426)	17.0 (997)	0.050
Wheezing without cold	7.1 (1245)	9.8 (936)	0.030
Cough + sputum	6.3 (1423)	10.1 (1009)	<0.001
Wheezing with shortness of breath	10.6 (1467)	13.6 (1029)	0.028
Chest illnesses	5.8 (1509)	9.5 (1051)	<0.001
Chest illness with sputum	4.5 (1398)	7.8 (1020)	<0.001
Three or more illnesses with sputum	2.4 (1404)	4.5 (1006)	0.005
Measles	16.4 (1292)	17.5 (888)	N.S.(0.560)
Sinus trouble	4.9 (1248)	3.7 (859)	N.S.(0.243)
Bronchitis	22.0 (1325)	25.4 (903)	N.S.(0.070)
Asthma	9.8 (1261)	13.0 (868)	0.026
Pneumonia	12.9 (1307)	18.1 (901)	0.001
Ear infections	31.7 (1304)	32.6 (868)	N.S.(0.683)
Allergy	15.9 (1493)	19.1 (1018)	0.043

\* Number of children in parentheses.

\* P > 0.05 is considered as N.S.

dren (Colley and Brasser, 1980) showed a close association between air pollution and various respiratory indices in children. The Groupe Cooperatif PAARC (1982) also demonstrated that children growing up in SO<sub>2</sub>-polluted areas in France show a higher prevalence of upper respiratory symptoms.

TABLE 4  
RELATIVE RISK FOR RESPIRATORY SYMPTOMS AND DISEASES FOR SECOND AND FIFTH GRADE  
SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AS COMPARED TO HADERA  
(NONPOLLUTED AREA)

Respiratory symptom or disease	Hadera	Ashdod	P value (for area)
Cough without cold	1.00	1.47	0.049
Cough + sputum*	1.00	1.55	0.007
Chest illnesses	1.00	1.95	0.003
Chest illnesses + sputum	1.00	1.91	0.015
Bronchitis*	1.00	2.30	0.008
Asthma	1.00	2.66	0.039
Pneumonia	1.00	1.47	0.003
Respiratory diseases among siblings	1.00	1.54	0.002

\* The model does not fit very well (P value for model <0.1).

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Other cross-sectional surveys carried out among schoolchildren in different countries also showed an association between area of residence and prevalence of upper and lower respiratory tract illnesses (Colley and Holland, 1967; French *et al.*, 1973; Hammer *et al.*, 1976; Love *et al.*, 1981; Lunn *et al.*, 1967; Melia *et al.*, 1981; Mostardi *et al.*, 1981b; Toyama, 1964).

Ferris (1978a), in a review article, criticized most children studies, especially because of insufficient control of possible confounding factors, and because exposures for children were only estimated.

Lebowitz (1981) recommends spatiotemporal designs as useful strategies in surveillance of respiratory effects of point sources of pollution. In this study, we tried to estimate health effects in two communities with different pollution levels. We used a spatial approach in which multivariate statistical analyses were performed in order to control for possible confounding factors. As in other environmental studies, only estimates of exposure for children, based on community monitoring, were available.

Monthly average concentrations of  $\text{SO}_2$  in Ashdod are within the range of 10.6 and 45.2  $\mu\text{g}/\text{m}^3$ , with an annual average of about 30  $\mu\text{g}/\text{m}^3$ .

In their study, Love *et al.* (1981) demonstrated health effects among schoolchildren with air pollution levels similar to those measured in our study. Melia *et al.* (1981) could not show any relation between prevalence of respiratory illness and  $\text{SO}_2$  annual means ranging from 12 to 114  $\mu\text{g}/\text{m}^3$ . Other studies (French *et al.*, 1973; Groupe Cooperatif PAARC, 1982; Hammer *et al.*, 1976; Mostardi *et al.*, 1981b) indicate higher  $\text{SO}_2$  concentrations as threshold levels for aggravation of respiratory conditions.

It is possible that other pollutants, either separately or in combination with  $\text{SO}_2$  and  $\text{NO}_x$ , contribute to the observed health effects. Since no measurements of the concentrations of heavy metals and organics (herbicides, for example) are carried out in Ashdod, their contribution to the health status of the population is not known.

In our survey, we could show that chronic respiratory symptoms, and most pulmonary diseases, were significantly more common among children from the polluted area. The higher prevalence of only the chronic (and not the transient) respiratory symptoms can not be attributed to general tendency of the population in Ashdod to overreport respiratory conditions among their children.

It is of interest that the logistic models fitted for the respiratory conditions better demonstrate the interaction between the background variables and the respiratory diseases, rather than the interaction with respiratory symptoms. The relative risks calculated for respiratory symptoms in Ashdod children were found to be about 1.50, and those for pulmonary diseases within the range of 1.47 and 2.66, as compared with 1.00 for Hadera children.

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Nordvall, S.L., Eriksson, M., Rylander, E., Schwartz, B.  
"Sensitization of Children in the Stockholm Area to House Dust  
Mites" Acta Paediatrica Scand 77:716-720, 1988.

ABSTRACT: Atopic sensitization of children in the Stockholm area to house dust mites (HDM) was investigated in a case-control study. Sixty children with and 60 without positive skin prick tests for HDM were matched for age and sex. HDM-sensitized children had previously more often lived in other areas known to be mite infested than the control children. Sensitization to mites was related to dampness in the homes, but no significant relationship was found to the type of residence, frequent visits to a summer house in the archipelago or parental smoking. Dust samples from mattresses of the children with the strongest positive reactions to mites in skin prick tests and the respective controls were subjected to an enzyme immunoassay, to measure the content of the major allergens of the Dermatophagoids (D.) species *D. pterinysinus*, *D. farinae* and *D. microceras*. Mattress dust samples from the beds of HDM-sensitized children contained significantly higher HDM antigen concentrations than those from the beds of controls. Private houses contained significantly more HDM antigens than flats and 10 of 11 homes in which a dampness problem was recognized contained mite antigens. It is postulated that mite infestation is increasing in the area, energy-saving measures created improved conditions for HDM survival.

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## Sensitization of Children in the Stockholm Area to House Dust Mites

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**ABSTRACT.** Nordvall, S. L., Eriksson, M., Rylander, E. and Schwartz, B. (Department of Paediatrics, St. Göran's Children's Hospital, Stockholm, Sweden and Allergologisk Laboratorium, Copenhagen, Denmark). Sensitization of children in the Stockholm area to house dust mites. *Acta Paediatr Scand* 77: 716, 1988.

Atopic sensitization of children in the Stockholm area to house dust mites (HDM) was investigated in a case-control study. Sixty children with and 60 without positive skin prick tests for HDM were matched for age and sex. HDM-sensitized children had previously more often lived in other areas known to be mite infested than the control children. Sensitization to mites was related to dampness in the homes, but no significant relationship was found to the type of residence, frequent visits to a summer house in the archipelago or parental smoking. Dust samples from mattresses of the children with the strongest positive reactions to mites in skin prick tests and the respective controls were subjected to an enzyme immunoassay, to measure the content of the major allergens of the *Dermatophagoides* (*D.*) species *D. pterinysinus*, *D. farinae* and *D. microceras*. Mattress dust samples from the beds of HDM-sensitized children contained significantly higher HDM antigen concentrations than those from the beds of controls. Private houses contained significantly more HDM antigens than flats and 10 of 11 homes in which a dampness problem was recognized contained mite antigens. It is postulated that mite infestation is increasing in the area, energy-saving measures creating improved conditions for HDM survival. **Key words:** house dust mites, *Dermatophagoides*, allergen analysis, ELISA.

House dust mites of the genus *Dermatophagoides* (HDM) are known to be important allergens in cases of dust allergy (1, 2). The growth and survival of HDM are known to depend on climatic conditions, the most important being the humidity in the homes (2-8). For HDM survival a relative humidity (RH) of 55% is required and the optimal RH for HDM growth is known to be as high as 75-80%. Since climatic conditions thus greatly influence the quantities of HDM in house dust, considerable differences are found between different geographic regions (9, 10), between seasons (11, 12) and also between different houses (7).

The general climatic conditions in the Stockholm area are unfavourable for growth of HDM, the winters being cold, with a prolonged indoor heating season and an indoor RH that is generally much below the critical 55% for HDM survival. In a previous study (13) mite concentrations in house dust from this area were found to be very low and *Dermatophagoides* were virtually absent. Yet in our daily practice we see children who are obviously sensitized to HDM, as shown by positive skin prick tests and radioallergosorbent tests for these allergens. This study was undertaken to find out the causes of sensitization to HDM in our area.

### MATERIAL AND METHODS

The study comprised children who were attending the out-patient allergy clinic of St. Göran's Hospital in 1984-1986 for routine tests. Skin prick tests (SPT) were carried out in accordance with the Nordic guidelines (14); during the period January 1984 to November 1985 Pharmedin® 10000 BU (Pharmacia AB, Uppsala, Sweden) was used and from December 1985 onwards the tests were performed with allergen precoated lancets (Phazet®) from the same supplier. The wheal sizes were related to those of histamine hydrochloride 1 mg/ml. A panel of ten allergens was used: *Dermatophagoides pterinysinus* (D.pt.), *Dermatophagoides farinae* (D.f.), cat, dog, horse, timothy, *Cladosporium her-*

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barum, *Alternaria alternata*, birch and mugwort. Sixty-six children with a positive SPT reaction (1+ or more, minimal mean wheal size 2.5 mm with a flare) to either or both of the two *Dermatophagoides* species were included in the study. Another 66 children who had been tested during the same time period for suspected allergies but had negative SPT to both *Dermatophagoides* species in SPT served as controls. A total of 80 boys and 52 girls aged 3–17 years were included in the study. Matching was performed with respect to both age and sex.

**Questionnaire.** The parents were asked to complete a questionnaire concerning the children's previous environment, i.e. whether they had lived in mite-infested regions in southern Sweden or abroad. Questions were also asked about paternal and maternal smoking, type of residence—i.e. whether they lived in a private house or a flat—and whether the family frequented a summer house in the Stockholm archipelago. There was also a question as to whether dampness was recognized as a problem in their permanent home. Forms were completed for 60 matched pairs of children.

**Dust sampling.** A mattress dust sample was requested from the beds of those mite-sensitized children who had displayed at least one 3+ SPT reaction to either of the two HDM species or 2+ reactions to both, and also from the beds of the respective controls. Dust from houses where a moisture problem had been acknowledged was also collected. Sampling was performed as described by Mosbech & Lind (15), by the parents, using their usual vacuum cleaner and a specially designed nozzle with a thick filter paper (13). This was done in 1986 from the last week of September to the end of October. Out of 62 requested samples, 54 were obtained and analysed.

**Dust analyses.** Aqueous extracts were prepared as previously described by suspending each gram of the dust sample in 5 cc of 0.9% saline (16). The contents of HDM antigens were determined by an enzyme-linked immunosorbent assay (ELISA), using affinity purified monospecific antisera against the major mite allergens of three *Dermatophagoides* species: *pteronyssinus* (antigen Der p1, formerly Dp 42 or P1), *farinae* (antigen Der f1) and *microceras* (antigen Der m1) (17). Standard Quality HDM extracts from Allergologisk Laboratorium A/S, Copenhagen, Denmark, were used as reference allergen solutions. Standard curves were run simultaneously on each of the plates. Less than 0.1% cross-reactivity was observed between these species-specific antisera in the ELISA assay (17).

**Statistics.** Fisher's exact test was used for comparison of data for cases and controls obtained by the questionnaires. Non-parametric tests were used in the processing of data for dust antigen contents, paired tests for the matched case-control comparisons (Wilcoxon signed ranks test) and the Mann-Whitney test for other comparisons.

## RESULTS

**Questionnaire.** A significantly higher proportion of the children with positive SPT to HDM than of the controls, reported long stays in mite-infested areas abroad or in southern Sweden (Table 1). More mite-sensitized children than control children lived in private houses but this difference was not significant. The parents of mite-sensitized children acknowledged a problem of dampness in their home more frequently than those of the controls ( $p < 0.006$ ). The frequency of visits to a summer house in the archipelago was similar in the two groups. A higher proportion of the mothers of mite-sensitized children than of control children were smokers, but this difference was not significant ( $p < 0.16$ ).

Table 1. Data on environmental factors obtained from questionnaire

	Travel		Private house		Dampness in home		Summer-house		Mother smoker		Father smoker	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Case	32	21	28	29	11	46	12	45	22	35	12	44
Control	17	39	22	38	2	58	17	43	17	43	18	41
<i>p</i> values	<0.003		<0.12		<0.006		<0.24		<0.16		<0.18	

Cases (mite-sensitized children) compared with controls (children without sensitization to mites). Statistics: Fisher's exact test. Travel=children with and without frequent stays in southern Sweden or other mite infested areas.

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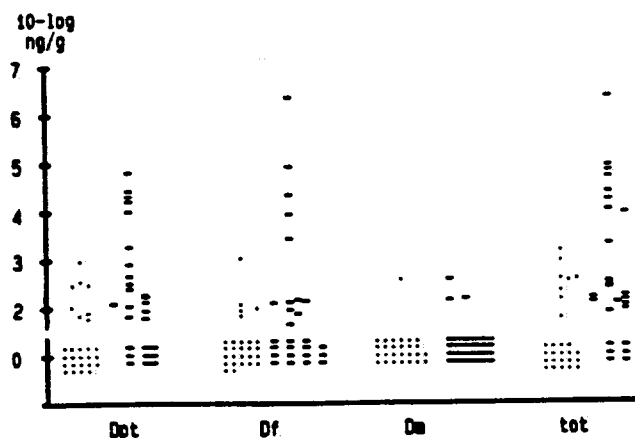


Fig. 1. House dust mite antigen contents from beds of mite-sensitized children (○) and controls (●). Dpt, Df and Dm = contents of antigens Der pI, Der fI and Der mI, respectively. tot = total amount of the three *Dermatophagoides* antigens.

**Dust analyses.** HDM antigens Der pI and Der fI were found in a considerable proportion of the dust samples, whereas antigen Der mI was found only sparsely. Dust from the homes of mite-sensitized children contained larger total amounts of mite antigens than dust from the homes of controls (Fig. 1) ( $p < 0.001$ ). This difference was significant both for Der pI ( $p < 0.02$ ) and for Der fI ( $p < 0.03$ ). The difference in mite antigen contents between private houses and flats (Fig. 2) was striking and was significant both for the total mite antigen contents ( $p < 0.001$ ) and for Der pI ( $p < 0.005$ ) and Der fI ( $p < 0.02$ ). A high proportion (10 of 11) of the dust samples obtained from houses where a dampness problem was recognized contained HDM antigens (Fig. 3).

#### DISCUSSION

From the results of this study two explanations emerge for the mite-sensitization observed among children in a Stockholm allergy clinic. One of them is obvious, i.e. previous residence in or frequent visits to other more heavily mite infested areas. The most important cause of the sensitization of the children, however, was the occurrence of HDM antigens in

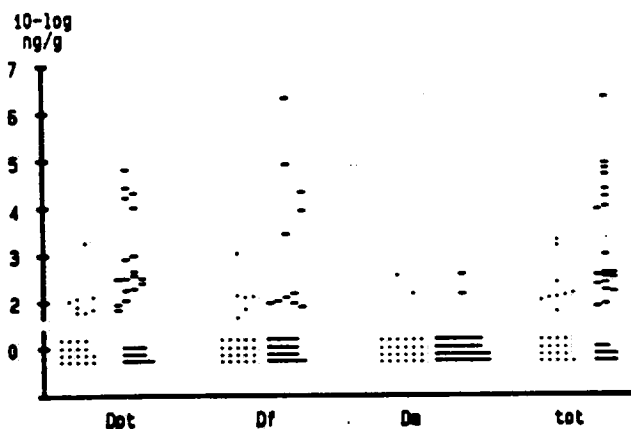


Fig. 2. House dust mite antigen contents from private houses (○) and flats (●). For further explanations, see legend to Fig. 1.

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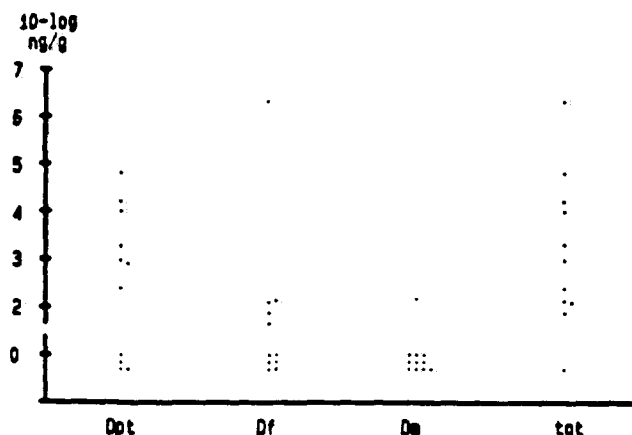


Fig. 3. House dust mite antigen contents in homes with acknowledged dampness problems. For further explanations, see legend to Fig. 1.

the dust of their homes. It is apparent from our data that the concentrations of HDM antigens may reach extreme peak levels in our homes.

In a previous study (13) *Dermatophagoides* were found to be very rare in the homes of the area. There may be several explanations for the divergent results of these two studies. In the previous study dust was collected from the homes of adults. A correlation between mite-sensitization in adults and the presence of HDM in their current homes is not expected to the same degree as in children, since adults are more likely to have been sensitized elsewhere and at a younger age. Further, in Tuross' study (13) dust was collected all through the year, whereas our samples were collected in the autumn, when peak levels could be anticipated. Microscopy was used in Tuross' study for the detection and quantification of mites, whereas we used a modern ELISA technique. These two techniques are not known to differ, however, when properly performed (17). Even though some differences in the design of the two studies may thus partly explain the discrepant results, it appears probable, that the difference reflects a true increase in HDM infestation in the area.

Increased mite infestation is a possible consequence of the changes in the construction of buildings that resulted from the energy crisis in the early seventies. Improved insulation and decreased ventilation of homes may have created a more favourable indoor climate for mite survival. Many homes in Sweden that were constructed in the late seventies smell of mould, but this problem occurs only rarely in older buildings and then often in conjunction with renovations (18). These findings are in accordance with the hypothesis that mite infestation of homes has increased and that the consequent sensitization to mites and clinical mite allergy may be of increasing importance in our area. Our findings, that private houses are more prone to mite infestation than flats, and the observed and very likely relation to problems of dampness, add further support to this notion.

In a majority of the dust samples HDM antigens were not detectable by the ELISA technique. This contrasts with findings from Copenhagen, where only a minority of the houses were found to be free of HDM antigens, when the same ELISA technique was used to examine dust from unselected houses (17). The general climatic conditions are probably more favourable for mite growth in Denmark than in our area, where the indoor climate possibly has a greater impact. In Denmark too, however, there are considerable discrepancies in the concentrations of HDM in house dust between different houses (7, 17), which has been attributed in part to differences in housing conditions (7).

The spread of HDM to houses of our temperate regions, where the general climatic con-

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ditions are unfavourable for mite growth, deserves further attention. Technical investigations of the types of houses that are associated with these problems seem important from a preventive aspect. Those who have already encountered this problem in their homes need technical advice to help them to eliminate mites. Studies performed in other regions of the world do not necessarily apply to our local conditions, and effects of improved ventilation and other measures for HDM sanitation should also be evaluated here.

#### ACKNOWLEDGEMENTS

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Mitchell, E.A., Stewart, A.W., Pattemore, P.K., Asher, M.I., Harrison, A.C., Rea, H.H. "Socioeconomic Status in Childhood Asthma", International Journal of Epidemiology 18(4): 888-890, 1989.

SUMMARY: This study examines the relationship between socioeconomic status (SES) and asthma prevalence and the use of asthma medication. One thousand and fifty European children aged eight and nine years were studied by parent completed questionnaire and histamine inhalation challenge. After controlling for sex of the child and for smokers in the house there were significantly higher lifetime ( $P = 0.029$ ) and current ( $P = 0.046$ ) prevalence rates of wheeze in children in low SES groups. There was no relationship between SES and asthma diagnosis, bronchial hyperresponsiveness (BHR:  $PD_{20} < 7.8 \mu\text{mol}$ ), or any combination of BHR with symptoms or diagnosis.

The use of bronchodilators and asthma prophylactic drugs was less frequent in the low SES groups of children with wheeze in the last 12 months both with concurrent BHR or irrespective of BHR than in those in high SES groups.

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# Socioeconomic Status in Childhood Asthma

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Mitchell E A (Department of Pediatrics, School of Medicine, University of Auckland, Private Bag, Auckland, New Zealand), Stewart A W, Pattemore P K, Innes Asher M, Harrison A C and Rea H H. Socioeconomic status in childhood asthma. *International Journal of Epidemiology* 1989, 18: 888-890.

This study examines the relationship between socioeconomic status (SES) and asthma prevalence and the use of asthma medication. One thousand and fifty European children aged eight and nine years were studied by parent completed questionnaire and histamine inhalation challenge. After controlling for sex of the child and for smokers in the house there were significantly higher lifetime ( $P = 0.029$ ) and current ( $P = 0.046$ ) prevalence rates of wheeze in children in low SES groups. There was no relationship between SES and asthma diagnosis, bronchial hyperresponsiveness (BHR: PD20  $< 7.8 \mu\text{mol}$ ), or any combination of BHR with symptoms or diagnosis.

The use of bronchodilators and asthma prophylactic drugs was less frequent in the low SES groups of children with wheeze in the last 12 months both with concurrent BHR or irrespective of BHR than in those in high SES groups.

For many diseases poor health is both more prevalent and more severe in children in families with low socioeconomic status (SES) than in children from better circumstances.<sup>1</sup> While some studies suggest that there is an excess of severe asthma in children with low SES,<sup>2,3</sup> several studies have suggested that there is a higher prevalence of asthma in children in high SES families compared with those in low SES,<sup>4,5</sup> and other studies have not found any relationship between asthma prevalence and SES.<sup>6,7</sup>

During a study comparing asthma prevalence between Australian and New Zealand schoolchildren<sup>10</sup> we have had the opportunity to examine the relationship between SES and the prevalence of childhood asthma using a number of different criteria for asthma (including bronchial hyperresponsiveness (BHR)) and the use of asthma medications. This study is reported here.

## METHODS

The methodology has been described in detail elsewhere.<sup>10</sup> Briefly a random sample of approximately 1300 European children was selected from the Auckland region.

A questionnaire was completed by the parents, which included questions about demographic details of the child and parents, a history of asthma symptoms, diagnosis, current medications for asthma, and parental or other household members' smoking habits. The children underwent a histamine inhalation challenge using the method of Yan *et al.*<sup>11</sup> Children whose forced expiratory volume in one second (FEV<sub>1</sub>) fell by more than 20% of baseline after receiving a cumulative dose of 7.8  $\mu\text{mol}$ s histamine or less were considered to have bronchial hyperresponsiveness (BHR). Socioeconomic status was defined from a revision of the Elley Irving socioeconomic six-point index for New Zealand occupations using the father's present or most recent occupation if he lived at home, otherwise the mother's occupation.<sup>12</sup> Five groupings were used (1-5) with group one representing the highest level and group five representing indices 5 and 6 combined.

Seven criteria for asthma prevalence were used for comparison with SES: any wheeze (including exercise wheeze) ever, any wheeze in the last 12 months and asthma diagnosed ever. The number of children with concomitant BHR in each category was also assessed. The seventh criteria was the presence or absence of BHR overall.

The current use of bronchodilators and asthma prophylactic drugs (inhaled steroids, cromoglycate) were examined by SES group in children with wheeze in the

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last 12 months, both with concurrent BHR or irrespective of BHR. Because of small numbers SES groups 1-2 and 4-6 were combined for this analysis.

The effect of the socioeconomic status of the children on the various measures of asthma was assessed by use of a logistic regression model. As it was thought that the smoking status of members of the household and the child's sex may have some confounding influence, these variables were also included in the model. Each of the asthma measures used were in the two category form, present or absent. Smoking was also classified as presence or absence of maternal smoker, paternal smoker or any smoker living in the household. The hypothesis considered was that there was a linear trend in the proportion of children with a positive outcome over the socioeconomic categories. With the size of sample available the power to detect an increase of 3.5% in outcome for each step from the highest socioeconomic category to the lowest was approximately 65 to 75%.

## RESULTS

Of those sampled (84%) 1084 children were tested. SES could not be ascertained from the questionnaires in 34 children, leaving a final sample size of 1050.

Table 1 gives the crude prevalence rates for the five SES groups for the seven chosen asthma criteria and the probability ( $p$ ) for a linear trend in SES after controlling for any smokers in the house and for sex of the child. A similar pattern of results is obtained regardless of whether the smoking variable being controlled for is mother's smoking, father's smoking or any smoker in the house. The lifetime or current prevalence rates for any wheeze (including exercise wheeze) are significantly higher in lower SES groups ( $p = 0.029$  and  $p = 0.046$  respectively), whereas there is no relationship between SES and the diagnosis of asthma, BHR or any combination of BHR with symptoms and previous asthma diagnosis.

Table 2 shows the prevalence of asthma medication use by SES group in asthmatic children using the criteria for asthma which include wheeze in the last 12 months. There is a clear trend for greater use of asthma medications in higher SES groups and this is particularly notable for prophylactic drugs.

## DISCUSSION

SES can be measured in a number of ways, the commonest being occupation, education or income. In other studies examining the relationship between SES and asthma prevalence the results have tended to be consistent irrespective of the measure of SES used. This study used occupation as the measure of SES.

The definition of asthma in previous studies has depended upon questionnaires and frequently upon parental reporting of asthma. In this study the parental questionnaire also sought information about wheezing, and the children were tested for BHR. The relationship between these factors and the diagnostic label 'asthma' is not straightforward. Furthermore, it is well established that asthma may be underdiagnosed.<sup>11</sup> Thus studies which have related asthma diagnosis to SES may yield different results from comparisons of symptoms and/or BHR to SES.

The higher prevalence of asthma diagnosis in high SES groups seen in earlier studies may reflect a SES effect on the disease label rather than the disease itself. This and other recent studies<sup>7,8</sup> have found no relationship between SES and asthma diagnosis, suggesting there may have been a change in the use of the label with time.

Studies defining asthma by wheezy symptoms have tended to find no relationship with SES.<sup>4,9</sup> In contrast this study found significantly higher rates of wheezy symptoms in children from lower SES groups. This is not explained by increased parental smoking in lower SES groups as the results were controlled for smokers in the household.

TABLE 1 Observed asthma prevalence (%) by socioeconomic group

	Socioeconomic group					Total (n=1050)	p value
	1 (n=124)	2 (n=299)	3 (n=344)	4 (n=205)	5 and 6 (n=78)		
Any wheeze/exercise wheeze ever	21.8	24.7	28.8	29.3	33.3	27.2	0.029
Any wheeze/exercise wheeze in the last 12 months	11.3	14.7	19.5	14.1	20.5	16.2	0.046
Asthma diagnosed ever	12.9	14.7	14.0	14.1	16.7	14.3	0.372
BHR on testing	21.0	20.4	21.8	18.0	19.2	20.4	0.903
BHR + any wheeze/exercise wheeze ever	10.5	11.4	13.7	10.7	12.8	12.0	0.379
BHR + any wheeze/exercise wheeze in last 12 months	8.1	8.0	11.9	7.3	10.3	9.3	0.412
BHR + asthma diagnosed ever	8.1	8.4	9.9	7.3	10.3	8.8	0.387



TABLE 2 Prevalence (%) of asthma medication by socioeconomic group in children using two definitions of asthma

	Socioeconomic group		
	1-2	3	4-6
Any wheeze/exercise in last 12 months	(n=58)	(n=67)	(n=45)
Bronchodilators	65.5	49.3	51.1
Prophylactic drugs	36.2	20.9	17.8
BHR and any wheeze/exercise wheeze in last 12 months	(n=34)	(n=41)	(n=23)
Bronchodilators	76.5	70.7	65.2
Prophylactic drugs	41.2	29.3	26.1

Some workers consider that BHR is useful for the diagnosis of asthma in epidemiological surveys as it is an objective test, most current asthmatics exhibit BHR and BHR correlates with the severity of asthma.<sup>14</sup> This study found no relationship between SES and BHR or any combination of BHR with symptoms and asthma diagnosis.

This study suggests there is no relationship between SES and asthma prevalence in children.<sup>6</sup> The finding of an increased prevalence of wheeze in low SES groups might be caused by an increase in the prevalence of factors which trigger or manifest wheezy episodes in the predisposed child. Such factors include respiratory tract infections,<sup>15</sup> which have been found to be more common in low SES groups, and house dust mites, which are found in higher concentrations in damp environments which probably occur more frequently in houses of poor families.

The finding of less frequent use of asthma medications in lower SES groups with current symptoms has been described<sup>16</sup> and is consistent with described social inequities in health.<sup>1,17</sup> There are a number of possible explanations for this finding. One possibility is that prescribing by the medical practitioner may vary according to the SES group of the child and their family. Alternatively there may be no difference in prescribing patterns, but rather a difference in uptake. Finally it may be that children with lower SES families have poorer, less regular and less frequent contact with medical practitioners and thus miss the opportunity for prescription of asthma drugs.

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Pope, C.A. "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley" AJPH 79(5): 623-628, 1989.

ABSTRACT: This study assessed the association between hospital admissions and fine particulate pollution ( $PM_{10}$ ) in Utah Valley during the period April 1985-February 1988. This time period included the closure and reopening of local steel mill, the primary source of  $PM_{10}$ . An association between elevated  $PM_{10}$  levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour  $PM_{10}$  levels exceeded  $150 \mu g/m^3$ , average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent. During months with mean  $PM_{10}$  levels greater than or equal to  $50 \mu g/m^3$  average admissions for children and adults increased by 89 and 47 per cent, respectively. During the winter months when the steel mill was open,  $PM_{10}$  levels were nearly double the levels experienced during the winter months when the mill was closed. This occurred even though relatively stagnant air was experienced during the winter the mill was closed. Children's admissions were two to three times higher during the winters when the mill was open compared to when it was closed. Regression analysis also revealed that  $PM_{10}$  levels were strongly correlated with hospital admissions. They were more strongly correlated with children's admissions than with adult admissions and were more strongly correlated with admissions for bronchitis and asthma than with admissions for pneumonia and pleurisy.

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# Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley

C. ARDEN POPE III, PhD

**Abstract:** This study assessed the association between hospital admissions and fine particulate pollution ( $PM_{10}$ ) in Utah Valley during the period April 1985–February 1988. This time period included the closure and reopening of the local steel mill, the primary source of  $PM_{10}$ . An association between elevated  $PM_{10}$  levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour  $PM_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$ , average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent. During months with mean  $PM_{10}$  levels greater than or equal to  $50 \mu\text{g}/\text{m}^3$  average admissions for children and adults increased by 89 and 47 per cent, respectively. During the winter months when the steel mill was open,  $PM_{10}$  levels

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## Introduction

On March 20, 1984, the US Environmental Protection Agency (EPA) proposed changes in the national ambient air quality standards for particulate pollution. Total suspended particulates (TSP) was to be replaced with a new indicator of particulate pollution that includes only those particulates with an aerodynamic diameter equal to or less than a nominal 10 micrometers ( $PM_{10}$ ). On July 1, 1987, the EPA announced its final decision. The previous primary TSP standards were to be replaced, effective July 31, 1987, with a 24-hour  $PM_{10}$  standard of 150 micrograms per cubic meter ( $\mu\text{g}/\text{m}^3$ ) with no more than one expected exceedance per year and an annual  $PM_{10}$  standard of an expected arithmetic mean of  $50 \mu\text{g}/\text{m}^3$ .<sup>1</sup>

Earlier studies of the health effects of particulate pollution<sup>2–4</sup> revealed a possible connection between air pollution and human health, and launched a wave of research exploring this connection.<sup>5–19</sup> Recent research has observed that even moderately elevated concentrations of particulate pollution may result in reductions in children's pulmonary function<sup>20,21</sup> and increased risk for bronchitis and other respiratory illnesses.<sup>22</sup> Other recent research questions the existence of a threshold level.<sup>1,23</sup>

Previous studies have not used  $PM_{10}$  as an indicator of particulate pollution. Recent experiences in Utah County have provided a unique opportunity to investigate a possible association between respiratory health and different levels of  $PM_{10}$ . Utah Valley has had daily monitoring of  $PM_{10}$  since April 1985; it has an extremely low percentage of smokers; it has experienced a prolonged shut-down and then reopening of the steel mill, its largest source of particulate pollution; over time, since monitoring of  $PM_{10}$  began, the valley has experienced considerable variability in levels of fine particulate pollution; and hospital inpatient admissions data for respiratory illnesses can be obtained. The objective of this paper is to report what has been observed in Utah Valley with respect to hospital admissions for respiratory illnesses and  $PM_{10}$  levels.

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## Methods

### Study Area

Utah Valley, located in Utah County of Central Utah, is the third largest county in the state with a population of 258,000 in 1987.<sup>24</sup> Approximately two-thirds of the population resides in five nearly contiguous cities situated on a valley floor with an elevation of approximately 1,402 meters above sea level bordered east and west by mountains (Figure 1).

Based on an unpublished 1986 Utah State Department of Health survey, only 5.5 per cent of Utah County's adults (18 years of age or older) smoke; approximately 90 per cent of its

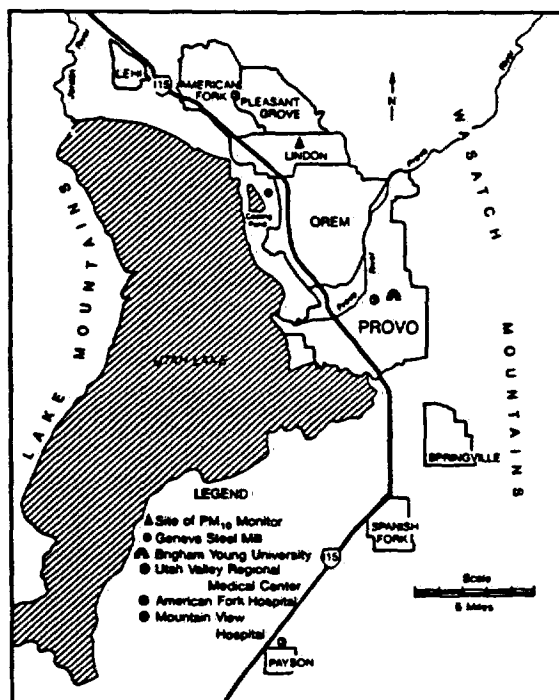


FIGURE 1—Study Area, Utah Valley

residents are members of the Church of Jesus Christ of Latter-Day Saints (Mormon)<sup>25,26</sup> which has strong church teachings against smoking.

Monitoring of particulate pollution began in 1964 and for carbon monoxide in 1971. On March 3, 1978, the EPA designated the county as a non-attainment area in accordance with provisions of Section 107 of the Clean Air Act. EPA ambient air quality standards for TSP and carbon monoxide were often exceeded at monitoring sites at Provo, Lindon, and Pleasant Grove during winter months when temperature inversions trapped emissions in stagnant air near the valley floor.

Generally, the county experienced improvements with respect to carbon monoxide pollution in the 1980s. At one monitoring site, the number of exceedances of the maximum eight-hour primary health standard for carbon monoxide fell from a high of 52 exceedances in 1982 to 10 exceedances in 1985. In order to continue to reduce levels of carbon monoxide pollution in the county, an automobile inspection/maintenance and anti-tampering program was implemented in 1986.

Particulate pollution levels in the county remained about the same from 1979-85. The 24-hour TSP standard of  $260 \mu\text{g}/\text{m}^3$  was exceeded as many as 10-18 times per year. The average annual geometric mean from 1979-85 for TSP at the Lindon monitor equalled  $65 \mu\text{g}/\text{m}^3$ . This mean level of TSP exceeded EPA's annual secondary standard of  $60 \mu\text{g}/\text{m}^3$  but not the annual primary health standard of  $75 \mu\text{g}/\text{m}^3$ . Monitoring of sulfur dioxides ( $\text{SO}_2$ ) was conducted in the county in the 1970s but was discontinued because  $\text{SO}_2$  levels were substantially below the annual primary health standard of .03 ppm, the 24-hour primary health standard of .14 ppm and the secondary 3-hour standard of .5 ppm.

The primary industrial source of fine particulate pollution as measured by  $\text{PM}_{10}$  in Utah County is the Geneva steel mill, commonly referred to as Geneva, located near Orem (Figure 1). When in operation, the mill emits approximately 82 per cent of all industrial sources of  $\text{PM}_{10}$  including power generation.<sup>27</sup> When all sources are accounted for, Geneva's contribution to  $\text{PM}_{10}$  equals 47 to 80 per cent of total emissions.<sup>27</sup> Other sources of  $\text{PM}_{10}$  include wood burning (approximately 16 per cent), road dust (approximately 11 per cent), diesel fuel and oil combustion (approximately 7 per cent). Also, Geneva's contribution to the county's industrial emissions of sulfur oxides, nitrogen oxides, hydrocarbons, and carbon monoxides are approximately 95, 98, 86, and 82 per cent, respectively.<sup>27</sup>

Geneva was built for the US Government in the early 1940s as part of the World War II effort. It was sold to US Steel Corp in 1946. On August 1, 1986, the Geneva steel mill shut down as a result of a labor dispute with USX Corporation (previously US Steel Corp.) The plant reopened on September 1, 1987 under a new owner, Basic Manufacturing and Technologies of Utah, Inc. In April 1985, the Bureau of Air Quality began to daily monitor  $\text{PM}_{10}$  at a site in Lindon (Figure 1) using a Sierra Anderson high volume sampler. During the winter season of 1985/86, Geneva was still open and 24-hour  $\text{PM}_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$  on 13 occasions. The highest single day concentration was  $365 \mu\text{g}/\text{m}^3$ . During the winter of 1986/87 while Geneva was shut down, 24-hour  $\text{PM}_{10}$  levels never exceeded  $150 \mu\text{g}/\text{m}^3$ . During the winter of 1987/88, following the reopening of Geneva, 24-hour  $\text{PM}_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$  on 10 occasions with a single day high at 223 (Figure 2).

During the winter of 1985/86, a random sample of county residents indicated that most residents thought that air quality was a serious problem and 29 per cent indicated that they had one or more members of their family who had health problems that were aggravated by air pollution.<sup>28</sup> During the winter of

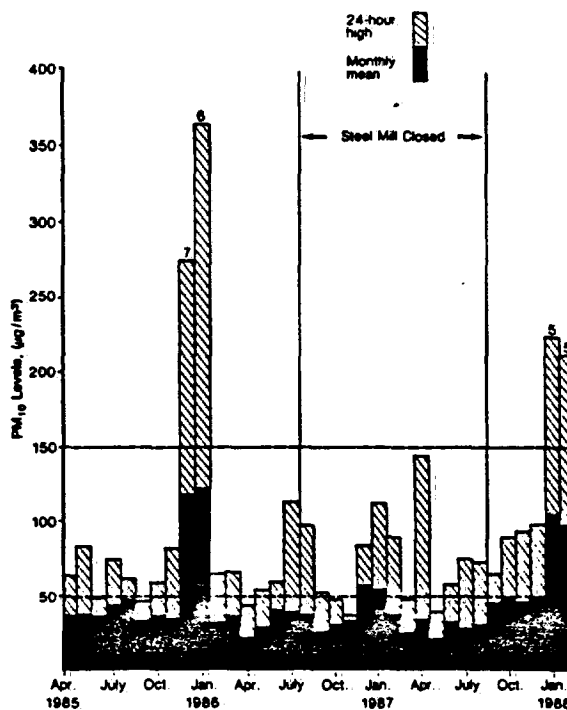


FIGURE 2—Monthly Mean and 24-Hour High  $\text{PM}_{10}$  (fine particulate pollution) Levels, Utah Valley, April 1985–January 1988

1987/88, following the closure and subsequent reopening of the steel mill, there was much local discussion about the contrast in air quality. The frequency and severity of respiratory illnesses were commonly perceived to have dropped when the mill was shut down, and then dramatically increased when it reopened. Newspaper articles, letters to the editor, and testimonials in public meetings often reflected this perception by many in the community.

#### Health Data

Hospital admissions data for respiratory-related illnesses were collected from April 1985 through February 1988. There were only four hospitals in the county. Data were collected from three of them that together had 579 beds. The other hospital in the County had only 20 beds, no pediatrics unit, no pulmonologist on its staff, and rarely provided inpatient care for respiratory illnesses.

A preliminary study of diagnosis-related groups (DRGs)<sup>29</sup> at Utah Valley Regional Medical Center indicated that DRGs 79, 80, and 81 (Respiratory Infections and Inflammations), DRGs 85 and 86 (Pleural Effusion), DRG 87 (Pulmonary Edema and Respiratory Failure), DRG 88 (Chronic Obstructive Pulmonary Disease), DRGs 92 and 93 (Interstitial Lung Disease), and DRGs 99 and 100 (Respiratory Signs and Symptoms) accounted for only 4.9, 0.6, 1.6, 3.3, 0.8, and 5.8 per cent of the collected cases, respectively. Initial comparative statistical analysis and regression analysis did not reveal any association between the closing and subsequent reopening of Geneva or  $\text{PM}_{10}$  levels and hospital admissions for any of these DRGs individually or collectively.

The bulk of the respiratory illness (83 per cent) were for the six DRGs that included 89, 90, and 91 (Simple Pneumonia and

Pleurisy) and 96, 97, and 98 (Bronchitis and Asthma) with 42 and 41 per cent of the cases, respectively. As a result, this analysis focuses on hospital admissions where the principal diagnosis was classified within one of these six DRGs.

Monthly admissions data for these six DRGs were compiled for each of the three hospitals. Records for outpatient and emergency admissions were not complete or consistent for the full time period. Therefore, only inpatient data were used in this analysis. Accurate records for Mountain View Hospital were available for the time periods April 1985 through September 1986 and January 1987 through February 1988. Accurate inpatient records for the other two hospitals were available from April 1985–February 1988.

#### Analysis Conducted

Utah Valley Regional Medical Center's admissions were sorted into in-county and out-of-county admissions. Both Utah Valley Regional Medical Center and American Fork Hospital are located within the central urban area of the county, near the major sources of pollution. The primary analysis used the combined Utah Valley Community Hospital in-county admissions and American Fork Hospital admissions as an indicator of the level of relatively severe respiratory illness in the urban area of the county.

Three other sets of hospital admissions data were used as control variables: "all-other" admissions from Utah Valley Regional Medical Center and American Fork Hospital, excluding in-county admissions for pneumonia, pleurisy, bronchitis and asthma; out-of-county admissions to Utah Valley Regional Medical Center for pneumonia, pleurisy, bronchitis, and asthma; and admissions to Mountain View Hospital in Payson for the same illnesses.

Hospital admission levels were compared across months with different levels of particulate pollution as measured by  $PM_{10}$ . Admission levels were also compared across comparable periods of time when the steel mill was open, closed, and then reopened. Finally, monthly hospital emissions were regressed on  $PM_{10}$  levels and weather variables obtained at Brigham Young University.<sup>30</sup>

#### Results

##### Comparative Analysis

As can be seen in Figure 2, there was considerable variability in  $PM_{10}$  levels in the county over the study period.

During those months when exceedances of the 24-hour  $PM_{10}$  standard of  $150 \mu g/m^3$  occurred, the number of admissions for children, 0–17 years of age, was nearly triple the number of admissions for months with no exceedances (Table 1). In adults, admissions were approximately 44 per cent higher during the months when exceedances occurred.

During months when the arithmetic mean  $PM_{10}$  levels were equal to or greater than  $50 \mu g/m^3$ , children admissions were nearly double than when the average  $PM_{10}$  levels were less than  $50 \mu g/m^3$ . Adult admissions were increased by approximately 47 per cent.

The above comparisons were complicated by the fact that the months with especially high levels of particulate pollution were during the winter, and the reason for the high incidence of respiratory illness may be at least partly attributed to winter weather. The intermittent operation of the steel mill provided the opportunity to compare different winter seasons with marked differences in  $PM_{10}$  levels. Figure 2 demonstrates that when the steel mill was closed,  $PM_{10}$  levels were relatively low. One concern about making observations pertaining to these time periods is that the winter when the Geneva steel mill was closed may have had relatively good weather conditions and limited conditions of stagnant air. Weather data indicated that temperatures fell below zero on only two occasions throughout the study period, both in January of 1988 when they fell as low as  $-1^\circ$  and  $-7^\circ$ . Snowfall during this time period for 1985/86, 1986/87, and 1987/88 totaled only 45.5, 33.5 and 27.5 inches, respectively.<sup>30</sup>

The National Weather Service computes an air stagnation or clearing index for valleys in Western Utah, including Utah Valley.<sup>31</sup> The index ranges from 0–1000 with lower values indicating more stagnant air. When the index is less than 200 pollution dispersal is "very poor" and weather conditions are such that air pollution potential is high. The month with the lowest average clearing index occurred during the winter the mill was closed. The average clearing index for the winter period of December–February for 1985/86, 1986/87, and 1987/88 was 388, 345, and 367, respectively, and the number of days when the index was below 200 for the same time periods equalled 47, 54, and 47, respectively.<sup>32</sup> Based on this index the air was relatively more stagnant and had higher air pollution potential during the winter when the mill was shut down than the previous or following winters.

Table 2 presents comparisons of hospital admissions be-

TABLE 1—Comparisons of Monthly Average Number of Hospital Inpatient Admissions for Utah Valley Regional Medical Center and American Fork Hospital across Months with Different Levels of  $PM_{10}$ <sup>a</sup>

Months Included	Number of Months Included	Mean $PM_{10}$ Level for Months Included	Mean High $PM_{10}$ Level for Months Included	Bronchitis and Asthma Ages 0–17	Bronchitis and Asthma Age 18+	Simple Pneumonia and Pleurisy Age 0–17	Simple Pneumonia and Pleurisy Age 18+	Subtotal Ages 0–17 <sup>b</sup>	Subtotal Age 18+ <sup>b</sup>	TOTAL <sup>b</sup>
All months	35	45.8 (4.3)	94.7 (11.9)	12.5 (1.6)	17.5 (1.0)	12.0 (1.5)	22.7 (1.6)	24.5 (2.8)	40.2 (2.3)	64.7 (4.5)
Months when 24-hour $PM_{10} < 150 \mu g/m^3$	31	37.5 (1.8)	72.3 (4.4)	10.5 (1.2)	16.9 (1.0)	9.9 (1.1)	21.4 (1.3)	20.4 (1.9)	38.3 (2.0)	58.6 (3.5)
Months when 24-hour $PM_{10} > 150 \mu g/m^3$	4	110.3 (5.5)	268.5 (35.0)	27.8 (6.7)	22.3 (2.9)	28.3 (4.6)	33.0 (8.1)	56.0 (11.1)	55.3 (10.0)	111.3 (14.0)
Months when mean $PM_{10} < 50 \mu g/m^3$	27	35.1 (1.3)	68.7 (4.6)	10.1 (1.3)	16.5 (1.1)	10.2 (1.2)	19.8 (1.2)	20.3 (2.1)	36.3 (2.0)	56.7 (3.9)
Months when mean $PM_{10} \geq 50 \mu g/m^3$	8	82.0 (11.0)	182.5 (36.4)	20.4 (4.4)	20.8 (1.8)	18.0 (4.5)	32.5 (3.9)	38.4 (8.5)	53.3 (5.1)	91.6 (10.0)

<sup>a</sup>Standard errors of the means are presented in parentheses.

<sup>b</sup>Total may not sum up exactly due to rounding error.

tween fall and winter periods when the steel mill was open, closed, and reopened. During the winter months from December to February, hospital admissions for children were approximately three times as high when the steel mill was open than when it was closed. Even during the Fall months (September–November) when no exceedances for the 24-hour primary health standard occurred, children admissions for bronchitis and asthma were approximately twice as high when the steel mill was open. Adult hospital admissions were not as obviously associated with the reductions of  $PM_{10}$  that accompanied the closure of the steel mill. There was, however, a notable increase in adult admissions following the reopening of the mill.

#### Regression Analysis

The results of some of the regression models are presented in Table 3. Model 1 regresses total monthly hospital admissions for pneumonia, pleurisy, bronchitis, and asthma on current and lagged  $PM_{10}$  levels. All lagged variables simply refer to the previous month's value. The results demonstrate a strong correlation between admissions and  $PM_{10}$ . In fact, 59 per cent of the variance in monthly admissions for these respiratory illnesses is explained by current and lagged monthly mean  $PM_{10}$  levels alone.

In Model 2, current and lagged mean low temperature variables were also included. This relatively simple linear model with only  $PM_{10}$  and temperature variables explains 83 per cent of the variance in total hospital admissions for these respiratory illnesses. The correlation between mean  $PM_{10}$  levels, mean low temperatures and hospital admissions is particularly striking when actual admissions and estimated admissions based on Model 2 are plotted together over time (Figure 3). Models 3–14 repeat the analysis done in Models 1 and 2 for total adult admissions, total children admissions, adult admissions for pneumonia and pleurisy, children admissions for pneumonia and pleurisy, adult admissions for bronchitis and asthma, and children admissions for bronchitis and asthma.

Autocorrelated errors exist with some of the models, particularly those with only  $PM_{10}$  levels as independent variables. This autocorrelation, however, is largely eliminated when weather variables are included. For example, the Durbin-Watson D statistic is 1.0 for Model 1 and 1.6 for Model 2. It is 1.3 for Model 3 and 2.0 for Model 4. There is also collinearity between  $PM_{10}$  levels and temperature. The correlation coefficient between the mean low temperature and monthly mean  $PM_{10}$  levels equals  $-0.32$ . This collinear-

ity complicates the analysis and makes specific best point estimators of the correlation coefficients difficult to estimate. However, Model 2 was reestimated using a nonlinear quasi-Newton iterative procedure which gave identical regression coefficients with somewhat smaller standard-errors.

Numerous other regression models were estimated that included snowfall, rainfall, evaporation, monthly mean temperatures, and mean high temperatures. The weather variable that was consistently most highly correlated with admissions was the mean low temperature. Regressions that used  $PM_{10}$  levels lagged for two months, and dummy variables that indicated the opening and closing of the steel mill and inversion seasons were also tried. Even with the inclusion of these other variables, strong, positive, correlations between hospital admissions and  $PM_{10}$  levels remained. Regression models were also estimated with monthly 24-hour high  $PM_{10}$  levels used as independent variables. The results were similar to those in Models 1–14 as presented in Table 3, but 24-hour high  $PM_{10}$  levels were generally not as strongly correlated with admissions as were the mean  $PM_{10}$  values.\*

#### Analysis with Control Variables

Neither comparative analysis nor regression analysis revealed any associations between the control variables and  $PM_{10}$  levels or the closing and reopening of the steel mill. "All-other" admissions that excluded in-county admissions for pneumonia, pleurisy, bronchitis, and asthma averaged 1,562 per month and appeared to be declining slightly over the study period. No seasonal variability nor any association with  $PM_{10}$  levels or the closing and reopening of the mill was observed. Monthly "all-other" admissions regressed on  $PM_{10}$  levels and temperature variables (Models 15 and 16 in Table 3) showed no significant correlation with  $PM_{10}$  levels.

Out-of-county hospital admissions to Utah Valley Regional Medical Center and admissions to Mountain View Hospital in Payson were regressed on  $PM_{10}$  levels and temperature variables. Models 17 and 18 in Table 3 present the results of the regressions for total out-of-county admissions for pneumonia, pleurisy, bronchitis, and asthma. The same regressions were also run on out-of-county and Mountain View Hospital with admissions broken down by adults, children, and respiratory illnesses, as done in Models 1–14.

\*Data available upon request to author.

TABLE 2—Comparisons of Hospital Inpatient Admissions for Utah Valley Regional Medical Center and American Fork Hospital across Time Periods with Geneva Steel Mill Open and Closed

Year	Steel Mill Open?	Mean $PM_{10}$ Level for Months Included	Mean High $PM_{10}$ Level for Months Included	Bronchitis and Asthma Ages 0–17	Bronchitis and Asthma Age 18+	Simple Pneumonia and Pleurisy Ages 0–17	Simple Pneumonia and Pleurisy Age 18+	Subtotal Ages 0–17	Subtotal Age 18+	TOTAL
Winter Months (December–February)										
1985/86	yes	90	235	78	75	76	73	154	148	302
1986/87	no	51	96	23	67	32	83	55	150	205
1987/88	yes	84	177	78	65	71	126	149	191	340
Fall Months (September–November)										
1985	yes	35	63	49	46	20	51	69	97	166
1986	no	31	47	23	48	25	60	48	108	156
1987	yes	47	83	55	46	24	66	79	112	191
Fall and Winter (September–February)										
1985/86	yes	63	149	127	121	96	124	223	245	468
1986/87	no	41	71	46	115	57	143	103	258	361
1987/88	yes	66	130	133	111	95	182	228	303	531

RESPIRATORY DISEASE AND COMMUNITY AIR POLLUTION<sup>1</sup>

TABLE 3—Sample Results of Multiple Regression Analysis

Model	Dependent Variable:	Regression Coefficients <sup>a</sup>					R <sup>2</sup>
		Constant	PM <sub>10</sub> Mean	Lagged PM <sub>10</sub> Mean	Low Temperature	Lagged Low Temperature	
1	Total	21.18 (7.1)	0.357 (.14)	0.599 (.15)	—	—	.59
2	Total	95.54 (12.8)	0.119 (.11)	0.339 (.11)	-0.351 (.30)	-0.929 (.31)	.83
3	Total Adult	25.31 (4.9)	0.150 (.09)	0.175 (.10)	—	—	.26
4	Total Adult	73.65 (9.4)	-0.016 (.08)	0.017 (.08)	-0.347 (.22)	-0.486 (.23)	.64
5	Total Child	-4.14 (4.0)	0.207 (.08)	0.425 (.08)	—	—	.67
6	Total Child	21.89 (9.7)	0.135 (.08)	0.321 (.08)	-0.004 (.23)	-0.443 (.24)	.75
7	Pn/Pi Adult	14.57 (3.5)	0.139 (.07)	0.034 (.07)	—	—	.19
8	Pn/Pi Adult	46.84 (7.3)	0.020 (.06)	-0.063 (.06)	-0.305 (.17)	-0.252 (.18)	.54
9	Pn/Pi Child	-1.50 (2.5)	0.112 (.05)	0.183 (.05)	—	—	.53
10	Pn/Pi Child	15.49 (5.3)	0.086 (.04)	0.095 (.05)	0.196 (.13)	-0.487 (.13)	.72
11	Br/As Adult	10.74 (2.0)	0.011 (.04)	0.140 (.04)	—	—	.36
12	Br/As Adult	26.81 (4.3)	-0.037 (.04)	0.081 (.04)	-0.042 (.10)	-0.234 (.11)	.59
13	Br/As Child	-2.63 (2.5)	0.094 (.05)	-0.241 (.05)	—	—	.60
14	Br/As Child	6.40 (6.5)	0.049 (.05)	0.226 (.06)	-0.201 (.15)	0.044 (.16)	.64
15	All-Other	1586 (46)	-0.050 (.9)	-0.604 (1.0)	—	—	.02
16	All-Other	1482 (120)	0.840 (1.0)	-0.798 (1.0)	5.904 (2.8)	-4.069 (2.9)	.15
17	Out-of-County Total	15.09 (2.9)	-0.047 (.02)	-0.006 (.03)	0.123 (.07)	-0.264 (.07)	.43
18	Mountain View Total	33.38 (6.8)	-0.013 (.05)	-0.041 (.06)	0.073 (.16)	-0.474 (.16)	.46

<sup>a</sup>The absolute value of the standard errors is provided in parentheses.

Pn/Pi = pneumonia/pleurisy

Br/As = bronchitis/asthma

Although Payson is located in the county and should be similarly influenced by contagious illness, it is over 32 kilometers from the major sources of pollution and should not be as influenced by monitored levels of PM<sub>10</sub>.

The regressions using out-of-county and Mountain View Hospital admissions are limited by the fact that only about 15 per cent of Utah Valley Regional Medical Center admissions are out-of-county, and Mountain View Hospital's data are missing for the months of October, November, and December of 1986. The results indicated that there was significant correlation between the mean low temperature lagged variable similar to those in the earlier regressions. There was no positive correlation between out-of-county or Mountain View Hospital admissions and PM<sub>10</sub> levels, however.

### Discussion

The results indicated that hospital admissions for respiratory illnesses were strongly associated with PM<sub>10</sub> levels. This association is much stronger for children than adults, and somewhat stronger for bronchitis and asthma than for pneumonia and pleurisy. These associations were particularly strong with monthly lagged variables suggesting that the health effects of particulate pollution are cumulative and that it takes time before they are manifested in inpatient hospital admissions data.

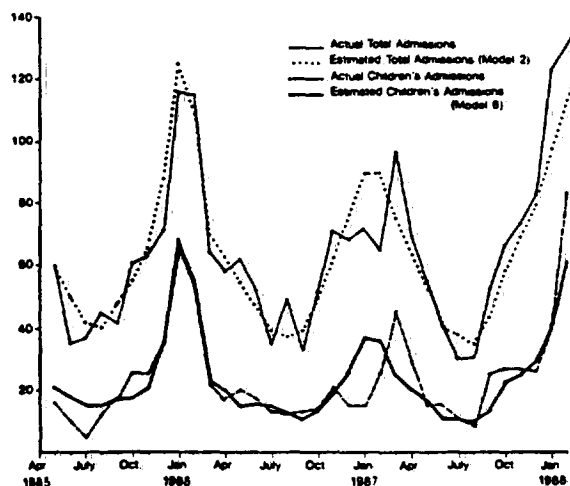


FIGURE 3—Actual and Estimated Hospital Admissions, April 1985 through January 1988, Utah Valley



Also, increased admissions for children are observed even for months when  $PM_{10}$  did not exceed  $150 \mu g/m^3$ , suggesting that this standard may not be adequate protection for some children.

There are several concerns about these observations. One concern is that if increases in contagious illnesses such as influenza by chance coincided with periods of high  $PM_{10}$  levels, particularly during the winters when the steel mill was open, then the observed correlation between  $PM_{10}$  and admissions may be spurious. It would be expected, however, that if this were the case, the same correlation would be found in hospital admissions from neighboring counties or communities unaffected by Utah Valley's principal sources of pollution. No such correlation was found for out-of-county admissions to Utah Valley Regional Medical Center or to Mountain View Hospital in nearby Payson. Nor was such correlation found between  $PM_{10}$  levels and non-respiratory hospital admissions.

Another concern is that often levels of several air pollutants rise and fall in concert.  $PM_{10}$  may be a surrogate for other air pollutants with which it is temporarily associated. Two pollutants that may have had similar impacts on respiratory illnesses during the study period are total suspended particulates and ozone. Because  $PM_{10}$  measures only relatively small particles of particulate pollution, and because it is the smaller particles that are expected to pose the greatest health risks, it is considered the most appropriate measure of particulate pollution as it relates to respiratory health.<sup>1</sup> Regression models estimated with monthly mean total suspended particulate levels used as independent variables yielded results similar to Models 1-14 presented in Table 3 which used  $PM_{10}$ . The correlations between admissions and total suspended particulates were generally not as strong as those between admissions and  $PM_{10}$ .

There was no evidence that suggested that  $PM_{10}$  was serving as a surrogate for ozone pollution. The only times ozone pollution in Utah Valley rose to levels of any consequence was in the summer months during hot sunny days, whereas the periods of high levels of  $PM_{10}$  and hospital admissions for respiratory illness occurred mostly during the winter months when the steel mill was in operation. The results of this study suggest that the dominant pollution in terms of its impact on respiratory health in Utah Valley is particulate pollution and that  $PM_{10}$  is a better indicator than TSP.

Finally, the association between respiratory illness and particulate pollution found in this study is relatively large as compared with some previous studies.<sup>20-22,33</sup> This relatively strong association can be explained in part because  $PM_{10}$  is a better indicator of particulate pollution as it relates to respiratory health than previously used indicators.<sup>1</sup> Also, because Utah Valley experiences relatively high levels of particulate pollution, yet has an extremely low portion of its population that smoke, particulate pollution is likely a relatively large contributor to respiratory disease in the county.

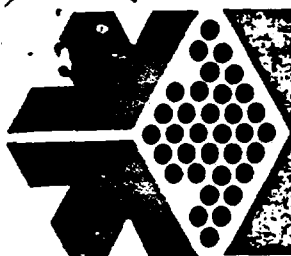
#### ACKNOWLEDGMENTS

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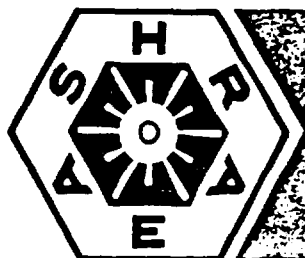
# IAQ89

Indoor Air Quality  
April 17-20, 1989  
San Diego, CA

## The Human Equation: Health and Comfort

*Organized by the*  
American Society of Heating,  
Refrigerating and Air-Conditioning  
Engineers, Inc.  
*and the*  
Society for Occupational and Environmental Health

IAQ89 **Manufacturers' Product and Service Session**



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# IAQ<sup>89</sup> THE HUMAN EQUATION: HEALTH AND COMFORT

## Welcome to IAQ '89

This year's conference has been organized by:

The American Society of Heating, Refrigerating and  
Air-Conditioning Engineers, Inc.  
and

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IAQ '89 is a follow up symposium to IAQ 86, 87 and 88, and  
will present demonstrated, documented solutions to indoor air  
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## UPCOMING ASHRAE MEETINGS

Winter	Date	Annual
	1989	Vancouver, BC June 24-28
Atlanta, GA Feb 10-14	1990	St. Louis, MO June 9-13
New York, NY Jan 19-23	1991	Indianapolis, IN June 22-26
Anaheim, CA Jan 25-29	1992	Baltimore, MD June 27-July 1

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## ASHRAE/SOEH IAQ'89 PROGRAM

**MONDAY, APRIL 17**

8:30 a.m. to 8:45 a.m.

### OPENING REMARKS

Aviary Ballroom

H.E. "Barney" Burroughs, IAQ'89 Chairman  
David S. Butler, ASHRAE President-Elect  
James A. Merchant, M.D., SOEH Past President

8:45 a.m. to 10:45 a.m.

### PANEL DISCUSSION:

#### GOVERNMENT ACTIVITIES IN INDOOR AIR QUALITY

Aviary Ballroom

James A. Merchant, M.D. Panel Chairman

### PANELISTS:

Sandra Eberle, US Consumer Products Safety Commission  
Richard W. Gorman, National Institute for Occupational  
Safety and Health  
James E. Hill, Ph.D., National Institute of Standards and  
Technology John Talbot  
George S. Malindzak, Ph.D., National Institute of En-  
vironmental Health Services  
David H. Mudarri, Ph.D., US Environmental Protection  
Agency  
Susan L. Rose, Ph.D., US Department of Energy

10:45 a.m. to 11:00 a.m. **BREAK**  
Foyer

11:00 a.m. to 12:30 p.m.

### TECHNICAL SESSION:

#### POLLUTANTS/HEALTH EFFECTS

Aviary Ballroom

Dean Baker, M.D., Session Chairman

#### Sick Building Syndrome Traced to Excessive Total Suspended Particulates (TSP):

C. W. Armstrong, M.D., F.A.C.P.  
P. C. Sherertz, Ph.D.  
G. C. Llewellyn, Ph.D., Virginia Department of Health, Rich-  
mond, Virginia

An epidemiologic and environmental investigation into the air quality of a high-rise, public office building was conducted in July, 1988. A walk-through inspection revealed particulate (dust) soiling of ceiling and work surfaces, in occupied sections of the service floor. Building air samples obtained by high-volume air pumps and cassette filters revealed elevated concentrations of total suspended particulates (TSP) which ranged up to 1.07 mg/m<sup>3</sup> [over 17 times the Building Officials and Code Administrators (BOCA) standard]. In 17 (59%) of the 29 areas tested, TSP levels exceeded the BOCA standard of  $\leq 0.06$  mg/m<sup>3</sup> (annual average). Recorded temperatures, relative humidity readings, and supply of outside air were within acceptable limits. Testing for volatile organic compounds, combustion products, formaldehyde, ozone, and fungal spores revealed no levels of concern. A survey of occupants in selected units was conducted with 94% participation. Fifty-five percent indicated that they had experienced symptoms that appeared or worsened during their working hours. Of these, 47% indicated that they had missed work because of their symp-

oms. Common symptoms were headache and sinus/upper respiratory congestion, compatible with air contamination by TSP or other irritants. In multivariate analysis, illness was found to be significantly associated with air TSP concentration ( $p < 0.002$ ), CO<sub>2</sub> concentration, average number of hours worked per week, gender, and smoking status. This is one of very few outbreaks of building-related illness where occupant illness has been associated with exposure to elevated levels of an environmental contaminant (TSP).

#### Symptoms and the Micro-Environment in the Sick-Building Syndrome: A Cross-Sectional Investigation:

L.M.J. Hodgson, M.D., M.P.H., University of Pittsburgh School  
of Medicine, Pittsburgh, PA  
P. Collopy, M.E., C.I.H., Carnegie Mellon University,  
Pittsburgh, PA

In a cross-sectional investigation in one building, complaints associated with the "sick building syndrome" were measured on a linear analogue scale questionnaire. At the same time, the micro-environment was characterized in the breathing zone by measuring temperature, relative humidity, respirable suspended particulates. Regression models suggested that heat load may have contributed to the level of complaints.

#### Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating With Woodburning Stoves:

J. S. Osborne, III, Ph.D. M.P.H., Southwestern Michigan Area  
Health Education Center, Kalamazoo, Michigan;  
R. E. Honicky, M.D., Michigan State University College of  
Human Medicine, East Lansing, Michigan

This study investigated a suspected relationship between the occurrence of chest illness in young children and use of woodburning stoves (WBS) for indoor heating. Data were prospectively collected during the winters of 1980, 1981, and 1982 for 62 mid-Michigan children age one to seven years (31 randomly selected children from WBS-heated homes and 31 controls from homes heated by conventional sources matched for age, sex, and place of residence). The specific a priori research hypothesis were that: the proportion of children having a chest illness would be significantly greater in the WBS-group than in the control group, that a greater proportion of WBS-group children would have chest illnesses lasting at least one week, and that a greater proportion of WBS-group children would be hospitalized before age two years for chest illness.

Results showed a significant difference ( $p < 0.05$ ) between the WBS and control groups in the proportion of children having a chest illness from 1980-82 (especially bronchitis, upper respiratory infection, and pneumonia); 39% of the WBS-group and 19% of controls had at least one such illness. Further, the WBS-group had a greater proportion of chest illnesses lasting at least one week (32% vs. 16%) and a greater proportion of hospitalizations for chest illness before age two years (16% vs. 10%). These differences were not accounted for by medical histories, frequency of physician visits, sociodemographic factors, or exposure to other sources of indoor air pollution investigated in the study (i.e., parental smoking, cooking with gas, urea-formaldehyde foam insulation) and suggest that indoor heating with WBS may be a significant risk factor for chest illness in young children.

#### The Effects of Environmental Tobacco Smoke on Acute Respiratory Disease:

B. D. Ostro, Ph.D., California Public Health Foundation,  
Berkeley, California

There are few sources of data that provide individual-level estimates of smoking status, as well as information on exposure

27

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Platt, S.D., Martin, C.J., Hunt, S.M., Lewis, C.W. "Damp housing, mould growth, and symptomatic health state" BMJ 298: 1673-1678, 1989.

**ABSTRACT.** Objective-To examine the relation between damp and mould growth and symptomatic ill health.

Design-Cross-sectional study of random sample of households containing children; separate and independent assessments of housing conditions (by surveyor) and health (structured interview by trained researcher).

Setting-Subjects' homes (in selected areas of public housing in Glasgow, Edinburgh, and London).

Subjects-Adult respondents (94% women) and 1169 children living in 597 households.

End points-Specific health symptoms and general evaluation of health among respondents and children over two weeks before interview; and score on general health questionnaire (only respondents).

Measurements and main results-Damp was found in 184 (30.8%) dwellings and actual mould growth in 274 (45.9%). Adult respondents living in damp and mouldy dwellings were likely to report more symptoms overall, including nausea and vomiting, blocked nose, breathlessness, backache, fainting, and bad nerves, than respondents in dry dwellings. Children living in damp and mouldy dwellings had a greater prevalence of respiratory symptoms (wheeze, sore throat, runny nose) and headaches and fever compared with those living in dry dwellings. The mean number of symptoms was higher in damp and mouldy houses and positively associated with increasing severity of dampness and mould (dose response relation). All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding. Other possible sources of bias that might invalidate the assumption of a causal link between housing conditions and ill health-namely, investigator bias, respondent bias, and selection bias-were also considered and ruled out.

Conclusion-Damp and mouldy living conditions have an adverse effect on symptomatic health, particularly among children.

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(500 IU) compared with 300 µg used in the Canadian work.<sup>1</sup>

Widespread administration of anti-D immunoglobulin antenatally in this regimen would not be possible at present because of limited supply from a decreasing pool of immunised donors. Immunoglobulin produced by genetic engineering, however, may be available soon, and trials are planned to study the effectiveness of even lower doses.

When studying a treatment regimen for any side effects it is important to avoid the bias created by considering only untoward consequences. Unexpected benefits are also possible, and we paid particular attention to any effects anti-D immunoglobulin may have had on the incidence of hypertensive disease such as pre-eclampsia. Some evidence suggests that previous blood transfusions may reduce the incidence,<sup>10</sup> and possibly some blood products also do so. The data collected, however, though not contradicting this hypothesis, showed no significant difference.

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(Accepted 10 April 1989)

## Damp housing, mould growth, and symptomatic health state

Stephen D Platt, Claudia J Martin, Sonja M Hunt, Chris W Lewis

### Abstract

**Objective**—To examine the relation between damp and mould growth and symptomatic ill health.

**Design**—Cross-sectional study of random sample of households containing children; separate and independent assessments of housing conditions (by surveyor) and health (structured interview by trained researcher).

**Setting**—Subjects' homes (in selected areas of public housing in Glasgow, Edinburgh, and London).

**Subjects**—Adult respondents (94% women) and 1169 children living in 597 households.

**End points**—Specific health symptoms and general evaluation of health among respondents and children over two weeks before interview; and score on general health questionnaire (only respondents).

**Measurements and main results**—Damp was found in 184 (30.8%) dwellings and actual mould growth in 274 (45.9%). Adult respondents living in damp and mouldy dwellings were likely to report more symptoms overall, including nausea and vomiting, blocked nose, breathlessness, backache, fainting, and bad nerves, than respondents in dry dwellings. Children living in damp and mouldy dwellings had a greater prevalence of respiratory symptoms (wheeze, sore throat, runny nose) and headaches and fever compared with those living in dry dwellings. The mean number of symptoms was higher in damp and mouldy houses and positively associated with increasing severity of dampness and mould (dose response relation). All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding. Other possible sources of bias that might invalidate the assumption of a causal link between housing conditions and ill health—namely, investigator bias, respondent bias, and selection bias—were also considered and ruled out.

**Conclusion**—Damp and mouldy living conditions

have an adverse effect on symptomatic health, particularly among children.

### Introduction

Showing a direct relation between damp housing and ill health is by no means straightforward. Firstly, those living in the worst housing conditions are likely to be experiencing other forms of adversity, such as low income and unemployment. Secondly, personal behaviour may also play a part in the causation of ill health. An equally important methodological concern is the process of the data collection itself. If information about health and housing conditions is elicited in the same interview respondents may exaggerate the prevalence of problems, leading to a spurious association between the two phenomena. Moreover, the researchers themselves may influence reporting.

In 1986 we carried out a preliminary study in Edinburgh, which attempted to overcome these methodological difficulties by using a double blind research design.<sup>1</sup> Children living in damp houses, particularly where there was also mould growth, were reported to have higher rates of respiratory and gastrointestinal symptoms, aches and pains, and fever than children in dry dwellings. These differences could not be attributed to smoking or differences between damp and dry households regarding unemployment, income, overcrowding, or duration of tenancy. The numbers of households that included a child was not large enough (n=101), however, to permit a full analysis of the role of other possible confounding variables. Accordingly, we carried out a larger scale, more detailed investigation.

### Subjects and methods

The study was conducted in three major cities: Edinburgh, Glasgow, and London. Within each city discrete geographical areas of public housing were

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identified in which (a) families with young children predominated; (b) the prevalence of damp housing was thought to be in the range of 25-50% of total dwellings; (c) socioeconomic state was likely to be fairly homogeneous; and (d) types of housing and structures of buildings, including any renovations, could be clearly specified. Two sites were chosen in Edinburgh, two in Glasgow, and one in London. Tenants' groups were contacted and their cooperation elicited. Lists of addresses at the chosen sites were obtained from the relevant housing departments. The intention was to achieve a sample of 500 eligible households in Edinburgh and in Glasgow and 200 in London. A random sample of addresses was drawn according to the total number of dwellings in the area.

Only those households with at least one child aged under 16 were eligible for inclusion in the study. As official statistics on the exact location of families with young children were not available the sample was identified in two ways: (a) at the time of the main health interview (see below) the interviewers identified suitable families by contacting each dwelling on the list; and (b) in two of the sites members of the tenants' association identified addresses on the list containing families who met the study criteria.

Two surveyors carried out an assessment of dampness (severity and type) and mould (severity and location) and details of the structure of the dwelling. Using an air sampler (Surface Air Systems) they extracted air samples from rooms and, where visible mould growth was present, a sample from each affected room was collected. A microbiologist estimated spore counts from the air samples and identified the fungi from air and walls when possible.

We devised and pretested two survey forms. The form for the house conditions survey contained items on type of building, location, number of rooms, dampness, mould, ventilation, insulation, and renovations. The health survey was a revised version of that used by Martin *et al.*<sup>11</sup> In the course of a structured interview the respondent (whenever possible the female householder) answered detailed questions about her own and her children's health during the past two weeks; smoking by all adults and children; type of heating, washing, and drying facilities; presence of pets; economic activity and occupation of all adults in the household; household income; and housing conditions and facilities.

The study was carried out during February-April 1988. Once the health interview had been completed the surveyors were instructed to visit the dwelling. The petri dishes containing air and wall mould samples were taken each day to the University of Strathclyde, where they were refrigerated and cultured. Air spore counts were calculated and fungi identified when possible. The surveyors and the microbiologist were blind to each other's findings and also to the findings of the health survey team.

We used four categorical independent variables relating to housing conditions. Households that received a house conditions survey were classified into three groups: those where there was no objective evidence of dampness or mould growth (dry), those with only damp, and those with mould (whether or not dampness was also present). The overall dampness in the household was calculated by averaging the score for each bedroom, sitting room, and kitchen on a four point scale of severity (0 = none; 3 = severe). Households in which the average dampness score exceeded zero (no dampness whatsoever) were divided into three approximately equal sized groups labelled mild (score ranging between 0.01 and 0.52), moderate (0.53 to 1.05), and severe ( $\geq 1.06$ ). A similar procedure was adopted to divide households into four groups differing in average severity of mould (none, mild (0.01 to

0.45), moderate (0.46 to 0.77), and severe ( $\geq 0.78$ )).

The spore concentration per m<sup>3</sup> air was measured in the kitchen, living room, and bedrooms of households in Edinburgh and Glasgow visited by the surveyors. On the basis of preliminary work in Edinburgh (B Flanagan and C A Hunter, unpublished data) and elsewhere<sup>12</sup> we devised a five point scale (coded 1 to 5): low ( $\leq 100$  viable spores/m<sup>3</sup> air), medium (101-300), high (301-1000), very high (1001-5000), and extremely high ( $> 5000$ ). The household spore concentration was the mean score on the scale per available room. A new variable was created by dividing this mean score into three groups: low (scoring 1), medium (1.01 to 2.00), and high ( $> 2$ ).

To ensure that the relation between housing conditions and ill health was not invalidated by covariation with other variables several possible confounding factors were also examined, particularly cigarette smoking in the household (no/yes), respondents' cigarette smoking (no/yes), net household income (above median (£80)/below median), overcrowding (less than/more than 1.5 people per room), employment in the household (somebody employed/nobody employed), and employment state of the respondent (employed/unemployed, no paid employment).

The respondent was asked to report on the presence of 16 specific symptoms seen in the past two weeks in any child (aged 0-15) living in the household. We devised two summary symptom scores relating to children: the unadjusted score being the total number of symptoms among all children in the household and the adjusted score being the total of symptoms divided by the number of children—that is, the mean number of symptoms per child. Another summary dependent variable for children was the mean score on health evaluation derived from the respondent's general evaluation of each child on a scale of 1 (excellent) to 5 (very poor). The respondent was also asked to report whether she had suffered from any of 17 specific symptoms over the past fortnight. A summary symptom score was merely the sum of individual symptoms. In addition, the respondent was asked to rate her general health on the same five point scale used for children and to complete the 30 item general health questionnaire (range 0-30), here used as a general indicator of psychological distress. Finally, we inquired about medical treatment for symptoms and the presence of a recurrent or longstanding illness among both respondents and children.

Univariate analyses of the relation between each independent variable and dependent variables were carried out with  $\chi^2$  tests (categorical variables) or one way analysis of variance (metric variables). Subsequently, multivariate analyses were performed to examine the association between housing conditions and ill health after controlling for possible confounding factors. When the response variable was binary/categorical we used logistic linear regression analysis; for metric response variables we used analysis of covariance. The extent of any dose-response relation between severity of dampness, mould growth, and air spore concentration and health was assessed by means of tau c (categorical variables) and the Pearson correlation coefficient (metric variables). Identical results were obtained with respect to metric variables transformed to base 10 logarithms. Only original values are reported below.

On the basis of previous work we expected to find a distinct effect of adverse housing conditions on respiratory and gastrointestinal symptoms in children and on emotional distress in adults. Evidence of a dose response relation was considered to be particularly relevant in assessing the likelihood of a causal impact of dampness and mould on symptomatic health.

For the purposes of this report the results from

Edinburgh, Glasgow, and London have been combined. (Although the prevalence of damp and mould varied in each city, there were no pronounced differences in the association between housing conditions and symptomatic health state between cities.)

## Results

### RATES OF RESPONSE

Of 1220 households with children eligible for inclusion in the study, a health interview was secured in 891 (73.0%); 156 (12.8%) respondents refused to be interviewed, and 173 (14.2%) could not be contacted. Surveyors completed their investigations of housing conditions in 597 households, constituting 48.9% of eligible households and 67.0% of those who had the health interview. A comparison between surveyed ( $n=597$ ) and non-surveyed ( $n=294$ ) households showed no differences in sociodemographic characteristics, such as gender, marital state, household size (including number of children), social class, and overcrowding, or regarding disposable income, cigarette smoking, length of time at current address, presence of pets, or self-reported damp or mould. The only significant difference concerned employment: 131 (22%) respondents in surveyed households were employed compared with 100 (34%) respondents in non-surveyed households ( $\chi^2=12.54$ ,  $df=1$ ,  $p<0.001$ ); corresponding figures for any adult in employment were 257 (43%) and 156 (53%), respectively ( $\chi^2=7.55$ ,  $df=1$ ,  $p<0.01$ ).

All subsequent analyses were based on the 597 households, containing 1169 children, that received both a housing survey and a health interview.

### COMPARISON OF THREE HOUSING CONDITIONS GROUPS

Out of the 597 households, only 184 (30.8%) were free from damp or mould (dry). In 139 (23.3%) households surveyors found evidence of damp and in 274 (45.9%, of which all but nine were also damp) actual mould growth was visible. The three housing conditions groups (dry, only damp, mouldy) were compared for descriptive purposes on a number of background (sociodemographic and other) variables. (It was, of course, recognised that a variable could act as a confounder even if it did not differentiate significantly between groups.) Only one significant difference emerged: respondents living in dry households had been living an average of 5.9 (SD 4.9) years at the address compared with 4.8 (4.1) years among respondents in damp houses and 6.4 (5.5) years among

respondents in mouldy houses ( $F=4.35$ ,  $df=2,584$ ,  $p<0.02$ ); only the difference between damp and mouldy houses was significant (Scheffe test,  $p<0.05$ ). Housing groups did not differ in number of children (mean (SD) 2.0 (1.0)), total number of household members (3.8 (1.2)), respondent's gender (559 (93.6%) women), respondent's marital state (384 (64.3%) married), net household income (293 (49.0%) under £80 per week), respondent's smoking (415, (69.5%)), any smoker in household (476 (79.7%)), respondent employed (136 (22.8%)), any household member employed (259 (43.4%)), overcrowding (109 (18.3%)), presence of pets (269 (45.1%)), tenure of last house (465 (77.9%) council dwelling), reasons for moving from last dwelling (90 (15.0%) because of dampness; 247 (41.4%) because of other problems with the house; 26 (4.3%) for health reasons), and use of Calor gas heating (81 (13.5%)). Respondents in mouldy households, however, reported more problems apart from the damp (especially noise, poor repair, and cold) than respondents in damp or dry households. (Mean (SD) problems 2.7 (1.5), 2.5 (1.6), and 2.2 (1.6), respectively;  $F=5.0$ ,  $df=2,594$ ,  $p<0.01$ ). In particular, the prevalence of cold as a problem was reported in 222 (81%), 100 (72%), and 114 (62%) households, respectively;  $\chi^2=20.4$ ,  $df=2$ ,  $p<0.001$ ).

### HOUSING CONDITIONS AND RESPONDENT'S HEALTH

Table I shows the relation between prevalence of symptoms in the respondent and housing conditions. Significant differences between groups were found regarding bad nerves, aching joints, nausea and vomiting, backache, blocked nose, fainting spells, constipation, and breathlessness. The lowest proportion reporting symptoms was found in dry households; with only one exception (fainting spells) the highest proportion was found in mouldy households. Although housing conditions were unrelated to the presence of any particular symptom, there was a significant variation in the total number of symptoms and in the respondent's evaluation of her health. In particular, those living in mouldy houses scored significantly higher than those living in dry conditions (Scheffe test,  $p<0.05$ ). The general health questionnaire score was not related to housing conditions (table I).

Preliminary univariate analyses had shown that only two of the possible confounding variables (respondent's economic position and cigarette smoking) were significantly associated with the presence or absence of individual symptoms. We therefore undertook a series of logistic regression analyses in which the dependent variables were the eight symptoms previously shown to be significantly associated with housing conditions. After controlling for the respondent's economic position and cigarette smoking these differences remained significant for all eight dependent symptom variables (problem free households always having the lowest proportion of respondents positive for symptoms).

The relation between housing conditions on the one hand and the total number of symptoms, health evaluation score, and general health questionnaire score on the other was further examined by means of analyses of covariance. After we controlled for length of time at address, other housing problems (or cold alone), respondent's economic position, respondent's cigarette smoking, and household income housing conditions remained significantly associated with the total number of symptoms (6 ranging between 0-10 and 0-14,  $p<0.05$  to  $<0.005$ ), with those living in mouldy households reporting most and those in dry households fewest symptoms. Housing conditions were not significantly associated with health evaluation score after we controlled for other possible con-

TABLE 1—Respondent's health during past two weeks by housing conditions. Figures are numbers percentages unless stated otherwise

Symptom	Housing conditions			Significance	
	No damp or mould ( $n=184$ )	Damp only ( $n=139$ )	Mould ( $n=274$ )	Degrees of freedom	p Value
Tiredness	76 (41.3)	69 (50.0)	141 (51.5)	4.84	0.089
High blood pressure	9 (4.9)	7 (5.1)	22 (8.0)	2.33	0.312
Persistent cough	30 (16.3)	27 (19.4)	64 (23.4)	3.47	0.177
Bad nerves	35 (19.0)	31 (22.3)	80 (29.2)	6.62	0.036
Wheezing	19 (10.3)	17 (12.2)	37 (13.6)	1.07	0.587
Aching joints	28 (15.2)	23 (16.5)	65 (23.7)	6.05	0.049
Skin problems	26 (14.1)	23 (16.5)	43 (15.7)	0.39	0.825
Persistent headaches	49 (26.6)	43 (30.9)	75 (27.4)	0.82	0.664
Nausea/vomiting	7 (3.8)	9 (6.5)	27 (9.9)	6.17	0.046
Backache	41 (22.3)	48 (34.5)	81 (29.6)	6.13	0.047
Blocked nose	25 (13.6)	18 (12.9)	58 (21.2)	6.53	0.038
Palpitations	8 (4.3)	9 (6.5)	22 (8.0)	2.44	0.295
Fainting spells	3 (1.6)	12 (8.6)	17 (6.2)	8.37	0.015
Diarrhoea	5 (2.7)	9 (6.5)	19 (6.9)	4.08	0.131
Constipation	11 (6.0)	8 (5.8)	33 (12.0)	7.08	0.029
Breathlessness	19 (10.3)	24 (17.3)	51 (18.6)	6.01	0.049
Feeling depressed	51 (27.7)	47 (33.8)	104 (38.0)	5.15	0.076
Any symptom	144 (78.3)	113 (81.3)	217 (79.2)	0.46	0.795
Mean (SD) No of symptoms	2.40 (2.37)	3.05 (3.01)	3.43 (3.25)	$F=6.67$	2.594 0.001
Mean (SD) health evaluation score	2.41 (0.93)	2.49 (0.99)	2.66 (0.97)	$F=4.09$	2.594 0.017
Mean (SD) general health questionnaire score	5.74 (7.12)	6.87 (7.78)	7.20 (8.35)	$F=1.92$	2.583 0.148

foundings variables, and the relation with the general health questionnaire score remained non-significant.

We examined the dose-response relation between the respondents' symptoms and increasing severity of dampness, mould growth, and air spore concentration. Table II summarises the findings of these analyses.

TABLE II—Respondent's health during past two weeks. Dose-response relation with damp, mould, and air spore count. Figures are tau values (*p* values) unless stated otherwise

Symptom	Dampness (Max n = 597)	Mould growth (Max n = 589)	Air spore count (Max n = 485)
Tiredness	0.09 (0.028)	0.06 (0.076)	-0.02 (0.341)
High blood pressure	0.04 (0.024)	0.04 (0.027)	0.05 (0.017)
Persistent cough	0.09 (0.010)	0.04 (0.110)	0.06 (0.062)
Bad nerves	0.07 (0.036)	0.09 (0.008)	0.08 (0.031)
Wheezing	0.05 (0.047)	0.03 (0.125)	0.01 (0.413)
Aching joints	0.05 (0.080)	0.07 (0.022)	0.06 (0.083)
Skin problems	0.03 (0.209)	0.00 (0.474)	0.06 (0.063)
Persistent headaches	0.04 (0.150)	-0.02 (0.279)	-0.11 (0.006)
Nausea-vomiting	0.04 (0.044)	0.05 (0.015)	0.02 (0.230)
Backache	0.04 (0.167)	0.02 (0.332)	0.11 (0.009)
Blocked nose	0.11 (0.001)	0.08 (0.005)	0.00 (0.451)
Palpitations	0.03 (0.096)	0.03 (0.051)	0.08 (0.001)
Fainting spells	0.05 (0.013)	0.01 (0.381)	-0.01 (0.289)
Diarrhoea	0.02 (0.146)	0.02 (0.109)	-0.01 (0.413)
Constipation	0.02 (0.271)	0.04 (0.054)	0.01 (0.414)
Breathlessness	0.09 (0.003)	0.05 (0.057)	0.08 (0.019)
Feeling depressed	0.06 (0.081)	0.08 (0.026)	0.06 (0.107)
Any symptom	0.02 (0.319)	-0.02 (0.299)	0.00 (0.482)
No of symptoms	<i>r</i> = 0.14 (0.001)	<i>r</i> = 0.09 (0.014)	<i>r</i> = 0.08 (0.039)
Health evaluation score	<i>r</i> = 0.07 (0.047)	<i>r</i> = 0.10 (0.008)	<i>r</i> = 0.05 (0.115)
General health questionnaire	<i>r</i> = 0.06 (0.082)	<i>r</i> = 0.06 (0.086)	<i>r</i> = 0.01 (0.414)

There was a significant tendency for increasing severity of dampness to be associated with a greater prevalence of the following symptoms: tiredness, high blood pressure, persistent cough, bad nerves, wheezing, nausea and vomiting, blocked nose, fainting spells, and breathlessness. The greater the extent of mould growth the higher the proportion of respondents reporting high blood pressure, bad nerves, aching joints, nausea and vomiting, blocked nose, and feeling depressed. Finally, the concentration of the air spores was positively associated with high blood pressure, bad nerves, backache, palpitations, and breathlessness and negatively associated with persistent headaches. Overall, the total number of symptoms tended to increase with higher degrees of dampness and mould and air spore concentration, while the health evaluation score was related only to severity of dampness and mould growth. No dose-response effect on the general health questionnaire score was evident.

Respondents living in the three different housing conditions were compared regarding action taken

during the past two weeks to deal with symptoms and presence of recurrent and long-standing illness. No significant differences were found.

#### HOUSING CONDITIONS AND CHILDREN'S HEALTH

Table III shows the prevalence of symptoms among children in the household by housing conditions. Significant differences were found regarding wheezing, sore throat, persistent headache, fever and high temperature, persistent cough, and runny nose. The highest proportion reporting these symptoms was always found in mouldy households; with only one exception (sore throat) the lowest proportion with symptoms was found in the dry households. Not only was there a significant difference in the proportion with any symptom (147 (79.9%) in dry households, 119 (85.6%) in damp houses, 248 (90.5%) in mouldy houses) but the mean number of symptoms (overall and per child) also differed significantly and in the same direction. The mean child health evaluation score was not significantly different between groups (table III).

In our preliminary univariate analyses we had noted that three of the possible confounding variables (overcrowding, any cigarette smoker, nobody employed) were significantly associated with presence or absence of individual symptoms. Another set of logistic regression analyses was therefore undertaken in which the dependent variables were the six symptoms previously shown to be significantly associated with housing conditions. After controlling for these three confounding variables differences remained significant for wheezing, sore throat, persistent headache, fever and high temperature, runny nose, and for any symptom. Only the main effect of housing conditions on cough was no longer significant.

The relation between housing conditions on the one hand and mean number of symptoms and mean health evaluation score on the other was further examined in a series of analyses of covariance. As before, we took into account differences in the length of time at address and other housing problems (or cold alone). We also added a control for the number of children in the household and the adult's general health questionnaire score (included because although it did not differ significantly with housing conditions, it was correlated highly with both the mean number of symptoms in children ( $r=0.30$ ,  $p<0.001$ ) and mean child evaluation score ( $r=0.35$ ,  $p<0.001$ )). Finally, we partialled out the effects of cigarette smoking in the household, unemployment, low income, and overcrowding. There was still a significant effect of housing conditions on the mean number of symptoms (6 ranging between 0.10 and 0.13,  $p<0.02$  to  $<0.005$ ). Children living in mouldy households were reported to have the highest number of symptoms and those living in dry households the fewest. Mean child evaluation score remained unrelated to housing conditions.

Table IV shows the dose-response relation between children's symptoms and increasing severity of dampness, mould growth, and air spore concentration. The more serious the dampness the greater the prevalence of bodily aches and pains, wheezing, vomiting, sore throat, irritability, tiredness, persistent headache, fever and high temperature, feeling depressed and unhappy, poor appetite, persistent cough, and runny nose. Dampness was also associated overall with the presence of any symptom. The more severe the mould growth the greater the likelihood of wheezing, sore throat, irritability, persistent headache, fever and high temperature, and runny nose. Mould growth was also associated with the presence of any symptom. The greater the air spore concentration the greater the prevalence of wheezing, irritability, and fever and high temperature.

TABLE III—Children's health during past two weeks by housing conditions. Figures are number (percentages) unless stated otherwise

Symptom*	Housing conditions			Significance	
	No damp or mould (n = 184)	Damp only (n = 139)	Mould (n = 274)	Degrees of freedom	<i>p</i> Value
Bodily aches-pains	23 (12.5)	30 (21.6)	43 (15.7)	4.90	2 0.086
Diarrhoea	34 (18.5)	30 (21.6)	50 (18.2)	0.73	2 0.694
Wheezing	30 (16.3)	26 (18.7)	74 (27.0)	8.41	2 0.015
Vomiting	22 (12.0)	25 (18.0)	52 (19.0)	4.18	2 0.124
Sore throat	56 (30.4)	34 (24.5)	116 (42.3)	14.99	2 <0.001
Irritability	23 (12.5)	28 (20.1)	56 (20.4)	5.32	2 0.070
Tiredness	25 (13.6)	28 (20.1)	48 (17.5)	2.55	2 0.279
Persistent headaches	23 (12.5)	19 (13.7)	58 (21.2)	7.16	2 0.028
Earache	27 (14.7)	15 (10.8)	47 (17.2)	2.95	2 0.228
Fever-high temperature	21 (11.4)	25 (18.0)	67 (24.5)	12.30	2 0.002
Feeling depressed-unhappy	20 (10.9)	25 (18.0)	42 (15.3)	3.45	2 0.178
Temper tantrums	37 (20.1)	37 (26.6)	74 (27.0)	3.13	2 0.209
Bedwetting	41 (22.3)	29 (20.9)	64 (23.4)	0.33	2 0.846
Poor appetite	31 (16.8)	37 (26.6)	68 (24.8)	5.49	2 0.064
Persistent cough	57 (31.0)	52 (37.4)	117 (42.7)	6.45	2 0.040
Runny nose	72 (39.1)	56 (40.3)	139 (50.7)	7.43	2 0.024
Any symptom	147 (79.9)	119 (85.6)	248 (90.5)	10.41	2 0.006
Mean (SD) No of symptoms	3.73 (3.95)	4.39 (4.63)	5.44 (5.19)	F = 7.56	2,594 <0.001
Mean (SD) No of symptoms per child	2.04 (1.98)	2.46 (2.36)	2.86 (2.43)	F = 7.23	2,594 <0.001
Mean (SD) health evaluation score	2.24 (0.89)	2.30 (0.91)	2.41 (0.94)	F = 1.98	2,592 0.140

\*Symptom present in any child living in household.

TABLE IV—Children's health during past two weeks. Dose-response relation with damp, mould, and air spore count. Figures are tau c values (p values) unless stated otherwise

Symptom	Dampness (Max n = 597)	Mould growth (Max n = 589)	Air spore count (Max n = 485)
Bodily aches-pains	0.08 (0.006)	-0.01 (0.383)	-0.01 (0.384)
Diarrhoea	0.02 (0.291)	-0.01 (0.386)	0.01 (0.361)
Wheezing	0.10 (0.005)	0.09 (0.005)	0.07 (0.044)
Vomiting	0.06 (0.029)	0.04 (0.106)	0.03 (0.238)
Sore throat	0.09 (0.020)	0.14 (<0.001)	0.03 (0.264)
Irritability	0.10 (0.004)	0.06 (0.040)	0.07 (0.033)
Tiredness	0.06 (0.043)	0.01 (0.365)	0.01 (0.351)
Persistent headaches	0.12 (<0.001)	0.09 (0.002)	0.08 (0.056)
Earache	-0.01 (0.349)	0.03 (0.170)	-0.04 (0.130)
Fever-high temperature	0.12 (<0.001)	0.10 (0.002)	0.06 (0.046)
Feeling depressed-unhappy	0.08 (0.007)	0.02 (0.237)	-0.02 (0.294)
Temper tantrums	0.04 (0.159)	0.06 (0.069)	0.01 (0.399)
Bedwetting	0.02 (0.313)	0.00 (0.460)	-0.01 (0.437)
Poor appetite	0.08 (0.015)	0.03 (0.200)	0.02 (0.336)
Persistent cough	0.11 (0.006)	0.06 (0.068)	0.05 (0.139)
Runny nose	0.08 (0.033)	0.09 (0.023)	0.06 (0.123)
Any symptom	0.08 (0.005)	0.07 (0.011)	0.00 (0.492)
Mean No of symptoms per child	r=0.17 (0.001)	r=0.14 (0.001)	r=0.11 (0.010)
Mean health evaluation score	r=0.13 (0.001)	r=0.12 (0.002)	r=0.05 (0.161)
Mean health evaluation score	r=0.08 (0.025)	r=0.07 (0.044)	r=0.06 (0.107)

Overall, the mean number of symptoms tended to increase with greater severity of dampness, mould growth, and air spore concentration, whereas the mean number of symptoms per child and the mean child health evaluation score were related only to greater doses of dampness and mould growth. The mean number of symptoms per child and the mean child health evaluation score were unrelated to the extent of air spore concentration.

The three groups of housing conditions were compared regarding the action taken to deal with children's symptoms during the past two weeks and presence of recurrent and longstanding illness. Children in mouldy households were more likely to have been given medicines (51.8%) than children in damp (43.2%) or problem free households (36.4%) ( $\chi^2=10.82$ ,  $df=2$ ,  $p<0.005$ ). Other differences did not reach significance.

## Discussion

Before offering an account of the role of damp and mould in the aetiology of symptoms it is necessary to consider four types of bias that may invalidate the assumption of a causal link between housing conditions and ill health—namely, investigator bias, respondent bias, selection bias, and omitted variable bias.

Investigator bias may be dismissed as housing conditions and the health of household members were independently assessed by two different groups of researchers, neither of which included the principal investigators. In addition, questionnaires were coded and data prepared by workers who were not familiar with the objectives of the study.

Some previous investigations of the housing-health relation, particularly those carried out by tenants' groups, have been criticised on the grounds that people living in damp and mouldy houses will be inclined to exaggerate the extent of their own and their children's health problems. A recent study suggested that the observed association between mould and respiratory symptoms may be accounted for by parental awareness of mould in the home.<sup>4</sup> Our reliance on informants' reports about the health of themselves and their children was deliberate. We were unconvinced about the reliability and appropriateness of diagnostic data derived from official records, especially those of general practitioners. We thought that it was valid to assess health state by means of self reported symptoms while at the same time recognising that the likelihood of respondent bias was thereby increased. This

problem was minimised, however, by the use of independent, expert assessments of housing conditions. Although subjective (self reported) and objective (expert) evaluations of the presence of damp and mould were significantly and positively associated ( $k=0.26$ ,  $p<0.001$ ), there was disagreement about damp and mould state in 183 (30.7%) of the dwellings. Furthermore, respondents could not have been aware of the air spore concentration in the building. (The association between self reported damp mould and spore count, although significant, was not high:  $r=0.14$ ,  $p<0.001$ .) Nevertheless, symptoms in both children and respondents were related to this measure. We also included the general health questionnaire score as a covariate when examining the effect of housing conditions among children as respondents with greater levels of psychological distress tended to report more ill health. The mean number of symptoms remained significantly higher in damp and mouldy dwellings than in dry dwellings. Thus though the overall number of symptoms may have been higher than would be obtained by an independent observer, there is no reason to believe that such a bias affected the main findings.

Another possible source of error is that of selection bias. People who already suffer from ill health may tend to live in damp or mouldy dwellings: symptoms may exist before, rather than be a consequence of, living in poor housing conditions. This could happen, for example, where the least desirable dwellings were allocated to those most in need who, by virtue of low income, social circumstances, or medical history, were more likely to report ill health. Although housing departments may not always act impartially in the selection of tenants to households, there is no evidence to suggest that they systematically allocate families in poorer health to damp and mouldy households. In this study families in damp and mouldy dwellings were not more likely to have come from previously poor conditions or to have moved for health reasons or to have lived a shorter period of time in the dwelling than families in dry houses. In addition, many of the children in all three housing groups were born in the household in which they were currently living. Thus selection bias is highly unlikely to account for the findings.

Omitted variable bias can arise when variables that are correlated with the major independent variable (in this case housing conditions) and have a significant (possibly causal) relation with the dependent (outcome) variable (such as symptom score) are excluded from the analysis. Whereas several factors were significantly associated with health state, only cold was also associated with housing conditions. Cold stress may have made some contribution to the experience of symptoms: a damp house is usually a cold house. Unfortunately, we were unable to assess the temperature of dwellings. We did, however, gather information on perceived coldness of the dwelling and this variable was included in the covariance analysis.

In summary, adult respondents living in damp and mouldy dwellings were more likely to report nausea, vomiting, constipation, blocked nose, breathlessness, backache, aching joints, fainting, and bad nerves than respondents living in dry dwellings. These differences remained after controlling for the respondent's economic position and cigarette smoking. In a more extensive covariance analysis respondents living in mouldy dwellings were found to have the highest number of symptoms even after taking account of possible confounding factors such as length of time at address, other housing problems, household income, economic position, and cigarette smoking. This analysis, however, showed that the respondent's subjective evaluation of health and psychological distress

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were both unrelated to housing conditions. Increasing doses of dampness and mould were especially linked to nausea, blocked nose, breathlessness, high blood pressure, and bad nerves and to a greater number of symptoms and a poorer health evaluation score.

For children, living in damp and mouldy dwellings was associated with a greater prevalence of wheeze, sore throat, runny nose, cough, headaches, and fever compared with those living in dry dwellings. With the exception of cough these differences were unaffected by the introduction of controls for smoking in the household, employment, and overcrowding. Additional possible confounding variables were added in an analysis of covariance, which still showed a significant effect of housing conditions on the mean number of symptoms among children in the household. A dose-response relation was particularly noted with respect to wheeze, sore throat, runny nose, irritability, persistent headache, and fever and high temperature. Increasing severity of dampness and mould and any symptom, the mean number of symptoms (overall and per child), and the mean child health evaluation score were also associated.

Several studies have suggested that some varieties of fungal spores are allergenic and give rise to respiratory conditions. Burr *et al* identified *Penicillium notatum*, *Cladosporium herbarum*, and *Aspergillus* species in the homes of asthmatic patients and found that the moulds gave positive skin test reactions for allergy.<sup>9</sup> Fungal spores are also believed to affect the respiratory tract by producing tissue lesions, by forming saprophytic colonies on mucus plugs, and by causing inflammation and irritation of nasal and bronchial passages and the alveoli.<sup>10,11</sup>

An investigation by May *et al* found symptoms of fever, muscular pain, chest tightness, cough, and headache to be directly caused by organic toxic dust and suggested that this "pulmonary mycotoxicosis" may represent a systemic reaction to inhaled fungal toxins.<sup>12</sup> Although their study was concerned with acute episodes after exposure to massive doses of organic dust, possibly similar, though less severe, symptoms occur as a chronic response to prolonged exposure to low concentrations of fungal toxins.

Analysis of the moulds collected from the dwellings in our study is still proceeding and a supplementary report on the relation of specific moulds to symptoms will be prepared. Single dwellings in the study were found to be harbouring over 15 species of mould and probably some of these would give rise to allergenic or toxic reactions, or both.

Emotional symptoms in children such as irritability and unhappiness are probably linked to physical symptoms and indicate that the mental health of children is also at risk. Some of the adults' symptoms are difficult to explain by reference to mould, though aching joints and nausea could both be reactions to fungal toxins. Reports of "bad nerves" are not surprising where living areas are unpleasant, children are sick, and family life may be fraught. Backache and constipation are puzzling phenomena and may be indirect consequences of conditions in the home. Breathlessness and blocked nose may be more closely related to low temperature. Increased blood pressure and hypoxia have been observed as reactions to cold stress.<sup>13</sup>

We have attempted at all stages of this study, which is probably the largest of its kind ever undertaken, to refute the null hypothesis—namely, that there is no relation between housing conditions and health state. To that end, we adopted double-blind interviewing procedures, included a wide array of possible confounding factors, and used multivariate statistical techniques. Having eliminated (as far as possible) alternative explanations for our findings, we concluded that damp and mouldy dwellings have direct deleterious effects on the physical and psychological well-being of adults and children. Our confidence in this conclusion is enhanced in more positive fashion by two observations: firstly, the similarity of these findings with those reported in our earlier study,<sup>1</sup> especially concerning children's respiratory symptoms; and, secondly, the strong relation between increasing doses of adverse housing conditions (dampness, mould growth, and air spore concentration) and symptoms of ill health, which is unlikely to be the result of respondent bias.

A considerable body of evidence now exists that supports the contention that dampness and mould is an important public health issue, not solely for its immediate impact but also for the longterm implications. Poor housing conditions in childhood, for example, are associated with higher rates of admission to hospital and higher morbidity and mortality in adult life.<sup>14</sup> Hopefully, planners, policy makers, and medical practitioners will now plan concerted joint action to eradicate this unacceptable and needless health risk.

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SUMMARY: This study examined the relationship between measures of home dampness and respiratory illness and symptoms in a cohort of 4,625 eight-to 12-yr-old children living in six U.S. cities. Home dampness was characterized from questionnaire reports of mold or mildew inside the home, water damage to the home, and the occurrence of water on the basement floor. Symptoms of respiratory and other illness were collected by questionnaire. Pulmonary function was measured by spirometry. Signs of home dampness were reported in a large proportion of the homes. In five of the six cities, one or more of the dampness indicators were reported in more than 50% of the homes. The association between measures of home dampness and both respiratory symptoms and other non-chest illness was both strong and consistent. Odds ratios for molds varied from 1.27 to 2.12, and for dampness from 1.23 to 2.16 after adjustment for maternal smoking, age, gender, city of residence, and parental education. The relationship between home dampness and pulmonary function was weak, with an estimated mean reduction of 1.0% in FEF25-75 associated with dampness and 1.6% with molds. We conclude that dampness in the home is common in many areas of the United States and that home dampness is a strong predictor of symptoms of respiratory and other illness symptoms among 8- to 12-yr-old children.

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# Home Dampness and Respiratory Morbidity in Children<sup>1-4</sup>

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## Introduction

Dampness in the home is a potential risk factor for respiratory illness in part through the action of (micro)organisms that thrive in damp environments. Dust mites (Pyroglyphidae) are a well-known source of allergenic substances (1-5). They thrive at relative humidities greater than 70%, and they are found in mattresses, carpets, and dust on surfaces moist enough to support them. Dust mites are most abundant at the end of the summer, after a prolonged period of high indoor humidity (6-10). They can survive low humidity conditions to a certain extent, but their numbers are reduced significantly in homes that are very dry in winter (10). The prevalence of mites and allergens in house dust decreases with increasing altitude (1, 11, 12), presumably because wintertime humidity is lower at higher altitudes. Few mites are found in dusts obtained in dry climates (13, 14). Murray and coworkers (15) reported a 10- to 20-fold increase in sensitization to mite extracts in children living in a damp climate when compared with children living in a dry climate. Sensitization to cat and dog dander was comparable to the two groups. Long before the house dust mite was shown to be responsible for allergy to house dust (1), it was known that asthmatics normally living at low altitudes suffered far fewer attacks at high altitudes, and that asthmatic patients generally had negative skin tests for dusts collected at high altitudes (16). Recently, an increased prevalence of asthma in Papua, New Guinea, has been associated with the increased use of blankets containing large numbers of dust mites (17).

Molds are another source of respiratory allergens (18-21). Mold species have critical relative humidities ranging from less than 80% to more than 90% (18). Some genera have stronger allergenic properties than do others, and within a genus, there can be considerable variation in allergenic potential among species (21). Mold growth in homes can cause severe respiratory disease requiring hos-

pitalization (22-24). Typical causes of abundant mold growth include leaks in the roofs or walls, urinating pets, improper carpet cleaning, leaky plant pots, and the use of a cold mist vaporizer (22-24). Molds are ubiquitous in ambient air, and in dry homes, the presence of molds appears mainly to be related to their presence in outdoor air (25). *Penicillium* and *Aspergillus* are among the molds typically found in residences (26-31). Within the allergic population, the prevalence of mold allergy has been estimated to be 2 to 30% (32).

Despite this information about the potentially harmful effects of home dampness on respiratory health, relatively few epidemiologic studies have investigated the health effects of dampness. A study from the United Kingdom reported an association in a group of about 200 children between the prevalence of respiratory symptoms and relative humidity in their bedrooms (33). Lesourd and coworkers (34) reported a trend toward increasing prevalence of cutaneous delayed-type hypersensitivity to a battery of ubiquitous antigens in white, Hispanic, and black schoolchildren. These investigators attributed this trend to the increased risk of exposure to microorganisms in poorer homes. Varekamp and Voorhorst (35) and Leupen (36) reported that patients with bronchial asthma were

more likely to live in damp homes than were control subjects.

This report utilizes information on home characteristics and respiratory health of children participating in a large, ongoing epidemiologic study of air pollution

**SUMMARY** This study examined the relationship between measures of home dampness and respiratory illness and symptoms in a cohort of 4,825 eight- to 12-yr-old children living in six U.S. cities. Home dampness was characterized from questionnaire reports of mold or mildew inside the home, water damage to the home, and the occurrence of water on the basement floor. Symptoms of respiratory and other illness were collected by questionnaire. Pulmonary function was measured by spirometry. Signs of home dampness were reported in a large proportion of the homes. In five of the six cities, one or more of the dampness indicators were reported in more than 50% of the homes. The association between measures of home dampness and both respiratory symptoms and other non-chest illness was both strong and consistent. Odds ratios for molds varied from 1.27 to 2.12, and for dampness from 1.23 to 2.15 after adjustment for maternal smoking, age, gender, city of residence, and parental education. The relationship between home dampness and pulmonary function was weak, with an estimated mean reduction of 1.0% in FEF<sub>25-75</sub> associated with dampness and 1.6% with molds. We conclude that dampness in the home is common in many areas of the United States and that home dampness is a strong predictor of symptoms of respiratory and other illness symptoms among 8- to 12-yr-old children.

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and respiratory health to explore the relationship between moisture in the home and respiratory symptoms in children.

## Methods

### Study Population

The study population consists of 6,273 schoolchildren living in six U.S. communities originally selected for their historic outdoor air pollution levels. These communities include Watertown, MA; Kingston and Harriman, TN; a geographically defined area in the southeast corner of St. Louis, MO; Steubenville and Mingo Junction, OH; Portage, Pardeeville, and Wyocena, WI, and a random sample of 50% of the schools in Topeka, KS.

Initially, approximately 1,000 children were enrolled in each city between 1983 (Watertown) and 1986 (Topeka). The cohort was drawn from the second through the fifth grades, with the number of grades depending on the size of the school population. Overall, 95.9% of the invited children participated. Sample sizes in participating communities varied between 832 (Watertown) and 1,135 (St. Louis). One year after the first examination, the children were invited to participate in a follow-up study. A total of 5,395 children participated, ranging from 735 in Watertown to 1,005 in Topeka. For 5,321 of these participants, both a questionnaire and a pulmonary function test were obtained. This report is based on the 4,625 white children who were 7 to 11 yr of age at the start of the study and who were seen again at the 1-yr follow-up examination.

### Health, Exposure, and Demographic Information

At both examinations, a questionnaire was given to each child to be completed by a parent or guardian and returned to school. Information regarding respiratory illnesses and symptoms was requested in a format equivalent to that recommended by the Epidemiology Standardization Project (37). Of the respiratory illnesses and symptoms, responses concerning doctor-diagnosed respiratory illness before 2 yr of age, bronchitis in the previous year, persistent cough (for 3 months of the year or more), persistent wheeze (most days or nights or apart from colds), chest illness that kept the child at home for 3 days or more, and an index of lower respiratory illness (bronchitis, cough, or chest illness) were considered. The questionnaire-based definition of these symptoms has been reported previously (38). In addition, the occurrence of doctor-diagnosed asthma in the past year has been considered, as home dampness appears to increase the presence of substances that cause and/or aggravate asthma. The occurrence of hay fever in the past year has been considered, as this may be indicative of the child's sensitivity to respiratory allergens. Other nonchest illnesses that restricted the child's activities for 3 days or more also were investigated, as molds may release biologically active substances that lead to systemic effects

(39). These other nonchest illnesses were defined by the question: "In the past year, has this child had any other major illness or accident that restricted his/her activities for a week or more?" This immediately followed the analogous question on chest illnesses.

The effect of home dampness on respiratory symptoms was evaluated separately for children with asthma or asthmatic symptoms. Persistent wheeze is often considered to be a marker for asthma in children. In this sample, more than half of the children with persistent wheeze did not report doctor-diagnosed asthma. Three groups of children were considered: children with doctor-diagnosed asthma, children with persistent wheeze but without doctor-diagnosed asthma, and children with neither asthma nor persistent wheeze.

In the initial as well as the follow-up questionnaire, information was asked about the family's smoking habits. Exposure to environmental tobacco smoke was expressed as the presence or absence of a mother who smokes in the home, a variable previously shown to affect childhood respiratory illness rates (38). Paternal smoking is highly correlated with maternal smoking, and it has been shown to affect childhood respiratory illness rates, although not as strongly as maternal smoking (38). Only maternal smoking was controlled in this analysis. The mean number of years of schooling of the parents (< 9, 9-12, > 12) was used as a proxy for socioeconomic factors that might influence respiratory health or symptom reporting.

The children were examined at school, where their weight and height in stockinged feet were measured. Forced expiratory maneuvers were performed on a recording spirometer (Survey Spirometer; Warren E. Collins, Braintree, MA) in a sitting position with free mobility without a noseclip. A detailed description of the measurement procedure has been given elsewhere (40).

In the follow-up questionnaire, three questions were included regarding potential moisture problems in the home: (1) Does water ever collect on the basement floor? (2) Has there ever been water damage to the building? (3) Has there ever been mold or mildew on any surface inside the home? From these, a fourth variable, home dampness, was created

(dampness absent if answers to questions 1 to 3 were negative, present if any were positive).

Indoor air pollution measurements, including humidity, were made in a stratified random sample of the homes of about 1,800 children (41). Relative humidity of the indoor air is less important for the growth of mites and fungi than the dampness of specific surfaces or parts of the building structure. These measurements will be reported separately.

The relationship between the questionnaire indicators of dampness and the respiratory health outcomes is the subject of this report.

### Statistical Methods

As a first step, symptom prevalences were calculated for each category of the home dampness variables. To investigate potential differences between cities, odds ratios were calculated for a number of relevant symptoms against the combined dampness variable for each city. In the next step, logistic regression models were constructed in which the association between home dampness variables and symptoms was adjusted for age, sex, parental education, maternal smoking, and city of residence.

Pulmonary function was measured by FEV<sub>1</sub>, FVC, and FEF<sub>25-75</sub>. The logarithm of each pulmonary function variable was regressed on an indicator of sex and on the logarithm of age, height, and weight plus maternal smoking, parental education, and indicator variables for the city of residence. Previously published analyses of pulmonary function of preadolescent children (40) have shown that this logarithmic transformation produces a linear relationship with constant variance. The residuals from these models were compared between categories of the home dampness variables by *t* test.

All statistical analyses were performed using the SAS Statistical Analysis System (42) on a Compaq 286 Deskpro personal computer.

### Results

Reporting rates for the different home dampness variables are given for each city in table 1. Molds and mildew were reported in almost 40% of homes in Kings-

TABLE 1  
REPORTING RATES FOR HOME DAMPNESS VARIABLES IN SIX U.S. CITIES

City	Reporting Rate for:			
	Molds (%)	Water Damage (%)	Basement Water* (%)	Dampness† (%)
Kingston, TN	38.1	12.1	11.3	45.7
Steubenville, OH	27.9	14.7	38.0	55.6
Watertown, MA	20.9	16.4	42.0	55.8
St. Louis, MO	26.9	23.0	39.4	56.4
Topeka, KS	33.0	22.2	30.0	56.9
Portage, WI	35.4	18.0	33.3	58.2

\* Includes homes with no basements.

† Dampness is defined as molds, water damage, or water in basement.

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TABLE 2  
SYMPTOM PREVALENCE FOR EACH OF THE HOME DAMPNES VARIABLE CATEGORIES

Symptom	Dampness Variable							
	Molds		Water Damage		Basement Water		Dampness	
	Yes	No	Yes	No	Yes	No	Yes	No
Wheeze	14.8	8.9	15.0	9.9	11.2	10.4	12.2	9.0
Cough	11.7	6.1	10.9	7.2	9.6	7.1	10.1	5.1
Bronchitis	11.1	7.0	10.3	7.8	7.9	8.5	9.0	7.4
Chest illness	10.7	7.7	11.4	8.0	10.0	7.9	9.9	6.8
Lower respiratory illness	24.5	16.2	23.8	17.7	20.8	17.9	22.0	14.8
Respiratory illness before age 2	12.3	8.4	10.8	9.3	10.0	9.4	10.8	8.1
Asthma	5.4	4.4	5.4	4.5	5.2	4.5	5.1	4.1
Hay fever	23.2	15.8	22.2	17.4	19.4	17.6	19.8	16.3
Nonchest illness	12.5	9.1	13.7	9.5	11.7	9.6	11.9	8.3

ton/Harriman, TN. Reporting rates in other communities ranged from 20.9% in Watertown to 35.4% in Portage. A high rate of water damage was found in St. Louis, MO (23.0%), and water was reported to collect occasionally in the basement in approximately 40% of the homes in Watertown, MA, St. Louis, MO, and Steubenville, OH. The low reporting rate in Kingston/Harriman, TN is partly related to the fact that few homes in the sample had basements (63.3% compared with 78.4% in Topeka and 93.7% to 98.3% in the other communities).

Children living in homes with indications of dampness had consistently higher rates of respiratory symptoms than did children living in homes without these indications (table 2). City-specific unadjusted odds ratios for the association between respiratory symptoms and dampness were remarkably consistent across the six communities (table 3). Similar patterns were found with the other measures of home dampness (results not shown). These city-specific values demonstrate a strong and geographically consistent association between dampness and most childhood respiratory symptoms.

When the data were combined across cities and adjusted for other predictors of respiratory symptoms, respiratory illness and symptoms, including asthma and hay fever and other nonchest illnesses, had associations with molds varying from 1.27 to 2.12 and with dampness varying from 1.23 to 2.16 (table 4). All but one of these associations were statistically significant, although the association was weakest for asthma. Similar results were obtained for water damage and water in the basement.

To assess the effects of asthma and wheeze on the association between home dampness and other respiratory symptoms, the population was stratified into

three groups: doctor-diagnosed asthmatics, wheeze without doctor-diagnosed asthma, and children with neither wheeze nor asthma. The results for molds, expressed as prevalence ratios, are given in table 5. Prevalence ratios were used for this comparison because wide variations in prevalence in the unexposed groups made odds ratios difficult to interpret. Ratios were consistently smallest among asthmatics, but this is explained in part

by the higher reporting rates among children not exposed to dampness.

After adjusting for age, height, weight, sex, city of residence, parental education, and maternal smoking, there was no difference in level of FEV<sub>1</sub> or FVC with the presence of home dampness (table 6). There was some indication that FEV<sub>25-75</sub> was negatively related to molds.

It could be argued that the excess of persistent wheeze among children living in damp homes was due to overreporting of symptoms by parents living in those homes. If such overreporting did occur, the group of children living in damp homes and reported to be symptomatic would be a healthier group than the symptomatic children living in dry homes. To investigate this issue, we investigated the relationship between persistent wheeze and pulmonary function separately for children living in homes with and without reported molds. Persistent wheeze was associated with an 8.5% deficit in FEV<sub>25-75</sub> (95% CI, 5.6% to 11.2%) among children in homes with no molds, and a 9.2% deficit (95% CI, 5.5% to 12.7%) in homes with molds af-

TABLE 3  
CITY-SPECIFIC ODDS RATIOS FOR EFFECT OF DAMPNES ON SELECTED RESPIRATORY ILLNESS SYMPTOMS IN SIX U.S. CITIES

City	Respiratory Illness Symptom				
	Wheeze	Cough	Bronchitis	Chest Illness	Respiratory Illness before Age 2
Kingston, TN	1.51	3.72*	1.66*	1.31	1.55*
Steubenville, OH	1.48	1.42	1.40	1.78*	1.42
Watertown, MA	1.57	1.74	1.77	1.57	1.72
St. Louis, MO	1.53	1.98*	1.19	1.56	0.94
Topeka, KS	1.40	2.48*	1.09	1.86*	1.77*
Portage, WI	1.23	2.00*	0.90	1.38	1.43

\*  $p < 0.05$ .

TABLE 4  
ASSOCIATIONS BETWEEN HOME DAMPNES AND SYMPTOMS OF CHILDHOOD RESPIRATORY AND OTHER ILLNESS, ADJUSTED FOR AGE, SEX, CITY OF RESIDENCE, PARENTAL EDUCATION, AND MATERNAL SMOKING, IN SIX U.S. CITIES

Symptom	Estimated Odds Ratios for	
	Molds	Dampness
Wheeze	1.79 (1.44, 2.32)*	1.23 (1.10, 1.39)
Cough	2.12 (1.64, 2.73)	2.16 (1.64, 2.84)
Bronchitis	1.48 (1.17, 1.87)	1.32 (1.05, 1.67)
Chest illness	1.40 (1.11, 1.78)	1.52 (1.20, 1.93)
Lower respiratory illness	1.57 (1.31, 1.87)	1.68 (1.41, 2.01)
Respiratory illness before age 2	1.42 (1.12, 1.80)	1.40 (1.11, 1.78)
Asthma	1.27 (0.93, 1.74)	1.42 (1.04, 1.94)
Hay fever	1.57 (1.31, 1.87)	1.26 (1.06, 1.50)
Nonchest illness	1.40 (1.13, 1.74)	1.55 (1.25, 1.93)

\* 95% confidence limits in parentheses.

TABLE 5  
ASSOCIATIONS BETWEEN REPORTED MOLDS IN THE HOME AND  
RESPIRATORY SYMPTOMS IN ASTHMATICS, NONASTHMATIC  
WHEEZERS, AND NONASTHMATIC NONWHEEZERS  
IN SIX U.S. CITIES

Symptom	Estimated Prevalence Ratios for:		
	Asthmatics (n = 214)	Nonasthmatic Wheezers (n = 291)	Nonasthmatic Nonwheezers (n = 3,799)
Cough	1.50*	1.73*	1.59*
Bronchitis	0.86	1.41	1.74*
Chest illness	1.20	1.46	1.13
Lower respiratory illness	1.20	1.37*	1.39*
Respiratory illness before age 2	1.07	1.13	1.31*
Hay fever	1.04	1.46*	1.38*
Nonchest illness	0.99	1.51	1.31*

\* p < 0.05.

TABLE 6  
ASSOCIATIONS BETWEEN HOME DAMPNES VARIABLE AND PULMONARY  
FUNCTION IN CHILDREN, ADJUSTED FOR AGE, HEIGHT, WEIGHT,  
GENDER, CITY OF RESIDENCE, PARENTAL EDUCATION, AND  
MATERNAL SMOKING, IN SIX U.S. CITIES (n = 3,855)

Home Dampness Variable	Pulmonary Function Variable	Percent Difference Associated with Home Dampness*
Molds	FVC	0.44 (-0.27, 1.15)†
	FEV <sub>1</sub>	0.03 (-0.75, 0.82)
	FEF <sub>25-75</sub>	-1.62 (-3.19, -0.02)
Water damage	FVC	0.25 (-0.61, 1.12)
	FEV <sub>1</sub>	0.35 (-0.59, 1.30)
	FEF <sub>25-75</sub>	0.46 (-1.49, 2.45)
Basement water	FVC	0.16 (-0.54, 0.87)
	FEV <sub>1</sub>	-0.14 (-0.92, 0.65)
	FEF <sub>25-75</sub>	-1.14 (-2.74, 0.44)
Dampness	FVC	-0.09 (-0.75, 0.58)
	FEV <sub>1</sub>	-0.21 (-0.93, 0.52)
	FEF <sub>25-75</sub>	-1.06 (-2.55, 0.44)

\* Difference in mean pulmonary function, expressed as percentage of the grand mean, between children living in damp homes and children living in dry homes.

† 95% confidence interval.

ter adjusting for age, sex, height, city of residence, parental education, and maternal smoking. FEV<sub>1</sub> was similarly reduced in children with persistent wheeze, irrespective of exposure to molds. Thus, children reported to have persistent wheeze had similar pulmonary function deficits whether they lived in dry or in damp homes, a result not consistent with the hypothesis of overreporting.

The questionnaire data were used to investigate the association between the home dampness variables and a number of potential determinants of home dampness: the use of humidifiers or dehumidifiers, heating system, type of building, and age of building. There were more dehumidifiers in use in homes where molds and mildew were reported (42.0 versus 28.7%). Molds and mildew were reported in 34.9% of detached single family homes (which constituted 76% of the total sample), and in 17.3% of two-family

homes (with 13% the only other major category). Molds and mildew were reported in 34.8 to 43.4% of homes built between 1940 and 1969, and in 26.1 to 31.9% of homes built either before 1940 or after 1969. Water damage was reported in 22.0% of the homes built before 1930 and in 9.9% of homes built after 1979, with increasing reporting rates with increasing age of the homes in between. Water in the basement was reported in 47.8% of homes built before 1930, decreasing gradually to a reporting rate of 11.2% in homes built after 1979. No other associations emerged from this analysis.

### Discussion

The results presented in this report suggest a consistent and strong association between reported dampness in the home and childhood respiratory symptoms. This association remained after adjust-

ment for city of residence, maternal smoking, age, sex, and parental education.

One explanation for these findings could be that people with children experiencing respiratory symptoms report dampness in their homes more readily than those whose children are not symptomatic. This seems unlikely, however, because the potential role of home dampness as a risk factor for respiratory illness has not received the public attention accorded to other risk factors such as parental smoking and the use of unvented combustion appliances.

Case studies (7, 10, 23) have documented increased mite populations and mold growth in damp homes. These organisms have, however, been associated primarily with causation and/or worsening of asthma. Interestingly, we find that reported asthma is the only respiratory symptom *not* consistently associated with dampness in the home. The symptom "persistent wheeze," which is closely associated with reported asthma in the data, is associated with dampness in the home. Also, the relationships with dampness were stronger among nonasthmatic children with or without persistent wheeze than among the asthmatic children (table 5). It could be argued that parents of children with doctor-diagnosed asthma tend to move or modify the home environment to make it as healthy as possible for their children.

The respiratory symptoms used in the analysis were strongly correlated. A child with one symptom was four times to more than ten times as likely to have one or more of the other respiratory symptoms than a child not having the index symptom. This makes it difficult to separate the associations between dampness in the home and the various respiratory symptoms. It is also possible that a relatively high percentage of children reporting symptoms other than wheeze or asthma have reactive airway disease. Hallett and Jacobs (43) reported that reactive airway disease was present in 80% of patients presenting with acute bronchitis. Molds have been associated with respiratory symptoms and diseases other than wheeze and asthma (23, 24).

A recent study in Edinburgh, Scotland found a highly elevated prevalence of respiratory symptoms among children living in damp homes (44). The prevalence of wheeze in the past year was as high as 38.1% in homes in which molds were reported to be present in the child's bedroom compared with 10.5% in homes where no molds were reported. There was no clear relationship between home

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dampness and bronchial lability, however, and this was interpreted as evidence that the association between home dampness and respiratory symptoms could be due to overreporting of symptoms (or a greater awareness of symptoms) among parents of children living in damp homes. The prevalence of wheeze was much higher in the damp homes in Edinburgh than in the damp homes in this study. In this study, the prevalence difference between homes with and without reported molds was only 6% (14.8 versus 8.9%). The mean of FEF<sub>25-75</sub> measurements was also lower among children living in damp homes, although only the association with molds was statistically significant. We also found that children with persistent wheeze had very similar deficits in FEF<sub>25-75</sub> and FEV<sub>1</sub> in dry and damp homes. Overreporting of wheeze in damp homes would have diluted the association between wheeze and pulmonary function level present.

Another interesting finding is the association between home dampness and reported illnesses other than those of the chest. Comparable associations have not been found in this population between smoking in the home and other nonchest illnesses (45). Nonchest illnesses may include various illnesses of the upper respiratory tract such as head colds, rhinitis, and sinusitis, which may be considered respiratory illnesses, and the association with dampness indicators is plausible. A recent study from the United Kingdom (46) has also suggested that home dampness is related to nonrespiratory symptoms.

These findings have implications both for further studies of indoor pollutants and for health policy. The effect of molds or dampness is comparable in size to the effect of passive smoking (44). Whether the respiratory illnesses produced by passive smoking and molds and dampness have similar long-term significance is unknown. Further investigation of childhood respiratory illnesses will require consideration of both of these variables simultaneously.

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Berwick, M., Leaderer, B.P., Stolwijk, J.A. "Lower Respiratory Symptoms in Children Exposed to Nitrogen Dioxide from Unvented Combustion Sources" Environment International 15: 369-373, 1989.

SUMMARY: A prospective epidemiologic study was carried out for 12 weeks in the winter of 1983 to evaluate the impact of indoor air contaminant levels on respiratory health. A group of 121 children below the age of 13 (59 with unvented kerosene space heaters in the home; 62 without) were enrolled in the study and nitrogen dioxide levels were measured in 93% of the subjects' homes for one two-week period. When socioeconomic status and history of respiratory illness were controlled, children under the age of seven exposed to 30 ug/m<sup>3</sup> or more of nitrogen dioxide were found to have a risk of reporting lower respiratory symptoms 2.25 times (95% C.I. 1.69-4.79) that of children who were not exposed. Aspects of our study design, including increased precision of exposure classification and the inclusion of very young children, may explain our findings.

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## LOWER RESPIRATORY SYMPTOMS IN CHILDREN EXPOSED TO NITROGEN DIOXIDE FROM UNVENTED COMBUSTION SOURCES

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A prospective epidemiologic study was carried out for 12 weeks in the winter of 1983 to evaluate the impact of indoor air contaminant levels on respiratory health. A group of 121 children below the age of 13 (59 with unvented kerosene space heaters in the home; 62 without) were enrolled in the study and nitrogen dioxide levels were measured in 93% of the subjects' homes for one two-week period. When socioeconomic status and history of respiratory illness were controlled, children under the age of seven exposed to  $30 \mu\text{g}/\text{m}^3$  or more of nitrogen dioxide were found to have a risk of reporting lower respiratory symptoms 2.25 times (95% C.I. 1.69-4.79) that of children who were not exposed. Aspects of our study design, including increased precision of exposure classification and the inclusion of very young children, may explain our findings.

### INTRODUCTION

Conflicting evidence exists for a relationship between low levels of nitrogen dioxide, such as those that commonly occur in homes with unvented combustion sources, and adverse health effects, such as increased respiratory illness (Keller et al. 1979; Lebowitz et al. 1983; Melia et al. 1977, 1979, 1982; Speizer et al. 1980; Ware et al. 1984). Much of the research has been constrained to measure exposure by proxy—the presence or absence of a source, usually a gas cooking stove. While obtaining environmental measurements of exposure has been difficult due to expense and the greater level of cooperation entailed by respondents, the assumption has not been justified that the presence or absence of an unvented gas appliance is sufficient to categorize

the exposure of a population. Nitrogen dioxide ( $\text{NO}_2$ ) levels in homes using electricity for cooking have been measured at levels as high as  $33.8 \mu\text{g}/\text{m}^3$  (Goldstein et al. 1979). A number of factors, such as ventilation rate and the presence of other unnoted unvented combustion appliances, are frequently difficult to measure and can cause this wide range in exposure levels.

To assess the existence and the magnitude of an association between  $\text{NO}_2$  levels and adverse respiratory outcomes, we wanted to capitalize on the increased use of kerosene heaters and their potentially high  $\text{NO}_2$  emissions. Because  $\text{NO}_2$  has been hypothesized to interfere with host defense mechanisms, lower respiratory illness, represented by symptom reports, was used to examine the association between

NO<sub>2</sub> and adverse health outcomes. Since acute respiratory infections are frequent, particularly among young children, greater power to detect differences in illness rates could be obtained from observing a relatively small number of subjects. In addition, reports in the literature indicated that young children would be most likely to be sensitive to any adverse effects from NO<sub>2</sub>.

## METHODS

### *Study design*

A prospective cohort study of adult women and children was conducted from January to April 1983 in New Haven, CT, to delineate associations between low levels of indoor air contaminant levels (including NO<sub>2</sub>, sulphur dioxide, and formaldehyde) and respiratory symptoms. A group of 121 children under the age of 13 was enrolled in this study, 59 living in homes with kerosene space heaters and 62 living in homes without heaters. To study the association between low levels of NO<sub>2</sub> and respiratory symptoms, we systematically chose one child from each family under the age of 13 and closest in age to 5. The participation rate was 78% of families living in homes with kerosene heaters, and 81% of those living in homes without heaters. The air monitoring design is described elsewhere (Leaderer et al. 1986).

### *Data collection*

Data were gathered from several sources: baseline in-person interviews, 6 follow-up telephone interviews, measurements from passive monitors placed in 93% of the homes, and town tax assessor record abstracts.

The baseline interviews were administered between October 1, 1982, and January 14, 1983, and gathered information on demographics, medical history, building characteristics, and homeowner's heating patterns.

Follow-up telephone interviews were administered bi-weekly from January 30, 1983, to April 2, 1983. These consisted of: (1) a symptom checklist covering 20 symptoms of upper respiratory illness, lower respiratory illness, symptoms of general malaise, and a count of the number of days with each symptom, and (2) current heating patterns.

Data abstracted from town tax assessor records included the assessed value of the home, the materials used, the condition of the home, its age, the type of heating system and fuel used, the number of rooms and floors in the home, and the square footage of the bottom floor.

Approximately 93% of the children's homes were monitored with passive diffusion tubes for NO<sub>2</sub> for at least one two-week period. These tubes were placed in three locations inside the residence and one location outside. Sulphur dioxide, formaldehyde, and air infiltration rates were measured in a subsample of homes, but will not be reported here.

### *Definition of respiratory illness*

The outcome variable of interest in this study was maternally reported acute respiratory illness, particularly lower respiratory illness. Lower respiratory symptoms included: fever, chest pain, productive cough, wheeze, chest cold, physician-diagnosed bronchitis, physician-diagnosed pneumonia, and asthma. Upper respiratory symptoms were also ascertained. They included: fever, sore throat, nasal congestion, dry cough, croup, and head cold. As the data were too sparse to analyze by individual symptom, clusters of lower respiratory symptoms and upper respiratory symptoms were formed, and incidence was summed for the entire study period of 12 weeks. A symptom cluster was considered present if two or more symptoms in the cluster were reported for one time period.

### *Definition of exposure*

Accurate classification of subjects by exposure to NO<sub>2</sub> was a major priority of this project. During the study, exposure definition was improved beyond the anticipated dichotomy, so that children, who were initially identified as exposed or unexposed as a function of living in a home with a kerosene space heater or not, were classified according to measured NO<sub>2</sub> levels. Since measurements were taken for only one two-week period, NO<sub>2</sub> levels were estimated for all other periods based on hours of use multiplied by the level of NO<sub>2</sub> estimated during burning. These estimates were not significantly different from the measured NO<sub>2</sub> levels which were determined to be the least biased indicator of household exposure to NO<sub>2</sub> and thus were chosen as the most refined exposure variable.

Personal exposure estimates indicated a 94% correlation ( $p < 0.01$ ) between monitors worn by a subsample of 23 adult subjects and the average estimate of the three monitored rooms in the household during the same time period. No higher correlation has appeared in the literature, and, in fact, Remijn (1985) reported that the household average NO<sub>2</sub> measurement is an excellent proxy for personal exposures.

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*Data analysis*

Data were edited for consistency, coded, and quality control measures undertaken as the data were entered. Unconditional logistic regression analyses were performed to determine the magnitude and statistical significance of each factor controlling for all other variables in the model. With the exception of age, all the independent variables were continuous. Age was treated as dichotomous—younger than seven years and seven years and older. It should be emphasized that this type of analysis allows only a general comparison of variables and is highly dependent on the choice of cutpoint. Adjusted odds ratios were calculated using the LOGIST procedure of the Statistical Analysis System (Harrell 1983). Similar techniques were also used to assess effect modification and statistical interaction.

**RESULTS***Demographic characteristics*

Comparisons were made among the 113 monitored children as well as the 8 who were not monitored. They were very similar. The mean age of the children was 6.7 years, and 82% were away from home approximately 6 hours per day in school or daycare. The average household size was 4.2, the average socioeconomic status was moderate (Hollingshead 4-fac-

tor index)—42.5, and all children were Caucasian. There were approximately equal numbers of boys and girls in each group.

*Measured household exposures to NO<sub>2</sub>*

Table 1 shows the measured NO<sub>2</sub> levels by each major category of NO<sub>2</sub> source: Kerosene Heater, Gas Stove, Gas Stove plus Kerosene Heater, and No Source.

*Health effects; Lower respiratory symptoms*

To assess the effect of NO<sub>2</sub> levels on the presence or absence of lower respiratory symptoms, while simultaneously controlling for effect modifiers and potential confounders, multiple logistic regression was carried out for the binary dependent variable, presence or absence of lower respiratory symptoms. Independent variables were included that had statistically significant relationships with respiratory symptoms in this study (SES, history of respiratory illness), and those which were cited in other studies as being important (household size, age, number of cigarettes smoked in the house per day, and exposure to NO<sub>2</sub>).

Children under the age of 7 who were exposed to 30 µg/m<sup>3</sup> NO<sub>2</sub> had an odds for being reported as having lower respiratory symptoms 2.25 (95% C.I. 1.69-4.79) times those of unexposed children the

Table 1. Measured NO<sub>2</sub> values (µg/m<sup>3</sup>) in homes of monitored children (n=113) by source presence, Yale Health and Heating Study, New Haven, CT, area, winter 1983.

	Kerosene Heater + Gas Stove n=6	Kerosene Heater Only n=49	Gas Stove Only n=13	No Source n=4
Kitchen	89.50	41.07	40.92	6.40
Living Room	76.00	43.40	24.85	6.23
Bedroom	104.75	38.33	28.54	5.19
House Average	90.08	40.93	31.43	5.94

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Table 2. Association between measured  $\text{NO}_2$  levels and reported lower respiratory symptoms, by multiple logistic regression analysis, in 113 monitored children in the Yale Health and Heating study, New Haven, CT, area, winter 1983.

Variable	Odds ratio	95% CI
Age	1.05	0.91-1.21
SES**	2.35	1.14-4.85
History of		
Respiratory Illness	1.29	1.03-1.62
Age < 7 *30 $\mu\text{g}/\text{m}^3$ $\text{NO}_2$	2.25	1.69-4.79
Age $\geq$ 7 *30 $\mu\text{g}/\text{m}^3$ $\text{NO}_2$	0.84	0.59-1.42

\*Hosmer goodness-of-fit:  $\chi^2 = 6.41$ , 6 d.f.,  $p=0.38$ .

\*\*20 units on the Hollingshead scale.

same age when the effects of a history of respiratory illness and SES were controlled (Table 2).

$\text{NO}_2$  exposure appeared to have no effect on reported lower respiratory symptoms in children aged seven or older. A history of respiratory illness and socioeconomic status contributed significantly and independently to the risk for reported lower respiratory symptoms. Children of higher socioeconomic status (20 units on the Hollingshead scale) were 2.4 times as likely as children of lower SES to be reported as having lower respiratory symptoms. A history of respiratory illnesses made the odds of reporting lower respiratory symptoms 1.3 times as likely in all the children. Exposure to environmental tobacco smoke was not significantly associated with reported symptoms in either age group.

## DISCUSSION

In this study the ability to measure acute effects at the same time as exposure seems to have allowed for more precise estimates of the associated health effects—in terms of lower respiratory symptoms, the range of the susceptible group (less than seven years old), and other potentially important risk factors. Since the previous literature has shown inconsistent results, it seems that the effect of  $\text{NO}_2$  is likely to be limited in many regards. It is plausible that there is a real biological effect, based on animal data and the trend toward seeing an effect in younger ages. Many

studies have reported that SES plays a significant role as does a history of previous respiratory illness (see e.g., Monto and Ullman 1974).

A major strength of this study was that misclassification of exposure was limited, though not entirely, by the individual household measurement of  $\text{NO}_2$  levels during one two-week period. If this study used dichotomous source classification (i.e., presence or absence of an unvented combustion source), as most research has been constrained to do, the association between lower respiratory symptoms and exposure would have been only marginally significant ( $p=0.08$ ). Thus, the qualitative nature of previous data may have obscured the ability to define association between  $\text{NO}_2$  and respiratory effects.

A limitation to the findings from this study is the currently unknown bias inherent in maternal reports of symptoms. However, we found no association between a mother's initial report of her child's propensity to illness assessed at baseline and subsequent reports of symptoms throughout the study.

## CONCLUSION

The study has demonstrated a statistically significant association between  $\text{NO}_2$  concentrations and the incidence of two or more lower respiratory symptoms in children under seven years of age. No such association was seen in older children. A history of previous respiratory illness and socioeconomic status

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were significantly and independently associated with reported illness. This research has important implications for the present and possibly future health of young children exposed to  $\text{NO}_2$  from any unvented combustion. The conclusions, however, are limited to this population and must be replicated, possibly with a population exposed to higher levels of  $\text{NO}_2$ , before they can be relied on as a basis for further action.

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Hurwitz, E.S., Gunn, W.J., Pinsky, P.F., Schonberger, L.B. "Risk of Respiratory Illness Associated with Day-care Attendance: A Nationwide Study" Pediatrics 87(1): 62-69, 1991.

ABSTRACT. The risk of respiratory and other illnesses in children (age groups: 6 weeks through 17 months, 18 through 35 months, and 36 through 59 months) in various types of day-care facilities was studied. Children considered exposed to day care were those who were enrolled in day care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before the interview; unexposed children were not enrolled in any regular child care with unrelated children and did not have siblings younger than 5 years of age receiving regular care with unrelated children. Although an increased risk of respiratory illness was associated with attending day care for children in all three age groups, this risk was statistically significant only for children 6 weeks through 17 months of age (odds ratio = 1.6; 95% confidence interval = 1.1 to 2.4) and children 18 through 35 months of age who had no older siblings (odds ratio = 3.4; 95% confidence interval = 2.0 to 6.0). In contrast, day-care attendance was not associated with an increased risk of respiratory illness in children 18 through 35 months of age with older siblings (odds ratio = 1.0). For children aged 6 weeks through 17 months, the exposure to older siblings was associated with an increased risk of respiratory illness; however, for children aged 36 through 59 months, older siblings were protective against respiratory illness. In addition, for the children in each age group currently in day care, increased duration of past exposure to day care was associated with a decreased risk of respiratory illness. It is estimated that during the period of the study approximately 10% of respiratory illnesses in the United States in children younger than 5 years of age were attributable to day-care attendance.

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# Risk of Respiratory Illness Associated with Day-care Attendance: A Nationwide Study

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**ABSTRACT.** The risk of respiratory and other illnesses in children (age groups: 6 weeks through 17 months, 18 through 35 months, and 36 through 59 months) in various types of day-care facilities was studied. Children considered exposed to day care were those who were enrolled in day care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before the interview; unexposed children were not enrolled in any regular child care with unrelated children and did not have siblings younger than 5 years of age receiving regular care with unrelated children. Although an increased risk of respiratory illness was associated with attending day care for children in all three age groups, this risk was statistically significant only for children 6 weeks through 17 months of age (odds ratio = 1.6; 95% confidence interval = 1.1 to 2.4) and children 18 through 35 months of age who had no older siblings (odds ratio = 3.4; 95% confidence interval = 2.0 to 6.0). In contrast, day-care attendance was not associated with an increased risk of respiratory illness in children 18 through 35 months of age with older siblings (odds ratio = 1.0). For children aged 6 weeks through 17 months, the exposure to older siblings was associated with an increased risk of respiratory illness; however, for children aged 36 through 59 months, older siblings were protective against respiratory illness. In addition, for the children in each age group currently in day care, increased duration of past exposure to day care was associated with a decreased risk of respiratory illness. It is estimated that during the period of the study approximately 10% of respiratory illnesses in the United States in children younger than 5 years of age were attributable to day-care attendance. *Pediatrics* 1991; 87:62-69; day-care facilities, respiratory illness.

**ABBREVIATIONS.** ARE, attributable risk in the exposed; PAR, population attributable risk; CI, confidence interval.

In recent years, interest has been growing in the possible health-related risks that result from the increasing use of day-care facilities in the United States. Among the illnesses of concern are infections of the upper respiratory tract, the most common cause of illness in children attending day-care facilities, as well as diarrheal illnesses, hepatitis, and *Haemophilus influenzae* infections. Infections of the upper respiratory tract, although typically mild, are of increasing interest because of their possible association with otitis media and associated complications.<sup>1,2</sup> We conducted a study to assess the risk of respiratory and other illness related to attending various types of day-care facilities. This study provided the opportunity to assess the risk of respiratory illness in children of various ages attending day-care facilities and to assess previously suggested characteristics of day-care exposure and their potential role in the risk of day-care-associated respiratory illnesses.

## METHODS

The study was designed to compare the rates of respiratory and other illnesses in exposed vs unexposed cohorts of children in each of three age groups: 6 weeks through 17 months (group 1), 18 through 35 months (group 2), and 36 through 59 months (group 3). Exposed children were defined as having child care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before interview. A child was considered unexposed if neither the child nor any siblings

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younger than 5 years of age had any regular child care with unrelated children during this interval. The study was designed to enroll at least 262 exposed and 262 unexposed children from each age group.

Children in the study cohorts were selected through a nationwide telephone survey that incorporated a random digit-dialing, cluster-sampling technique. A preliminary screener determined the age and exposure status of any children younger than 5 years of age in the household. The parents of all exposed children and a random sample of unexposed children (who were relatively more prevalent than exposed children) were subsequently administered an in-depth questionnaire which sought information including the occurrence of any respiratory or diarrheal illnesses and associated symptoms in children in the previous 2 weeks, exposure (both in and outside the home) to other children, immunization histories, and current and past child-care arrangements.

All interviews were conducted between March 12 and June 17, 1987. More than 35 000 households were called; 28 500 (81%) agreed to participate by completing the screening and when selected, the in-depth questionnaire. Of the participating households, 10% (2853) had children younger than 5 years of age. Of the 3475 children identified in these households, 29% could be classified as exposed, 60% as unexposed, and 11% did not meet the study definition of exposed or unexposed.

### Analyses

Primary analyses in this study focused on comparing the risk of respiratory illness among exposed and unexposed cohorts within 2 weeks before the interview; analyses were conducted separately for each age group. Although multiple children from the same household were enrolled in this study, one child at most (the youngest) from a given household was included in the analysis of each age group. This ensured that all the observations within each age group were independent; hence, standard statistical techniques could be used in each separate analysis. Comparisons of risk between age groups were conducted restricting the analysis to children without siblings.

To control for the effect of possible confounders and to identify potential interaction effects, we used multiple logistic regression analysis. Logistic models were developed as follows. For each age group, factors previously reported or suspected of being risk factors for childhood illnesses were screened by using Mantel-Haenszel statistics (see Table 1). The factors identified as potential con-

**TABLE 1.** Variables Considered for Multivariate Models

Region of country
Race (white, nonwhite)*
Income (<\$20 000)*
Mother's education (<high school)
Crowding (1 or more persons per room)
Work in day care or babysitting
Smoking at home by family members*
Siblings in household*
Current breast-feeding (age group 1 only)*
Month of interview*

\* Core variables selected for inclusion in model. (The variables without asterisks were not included in the model because eliminating them changed the exposure odds ratio by less than 5%.)

founders or interaction variables in any age group were selected as core variables, which were used in the logistic models for each of the three age groups. The variable "current breast-feeding" was used only in the youngest age group.

Logistic regression analyses were completed separately for each age group. The baseline logistic model included exposure, age, and the core variables as main effects. Two-way interaction terms involving exposure were then added to the baseline model stepwise (*P* value to enter, .05). Finally, the variables not involved in significant interactions were dropped from the model if their absence changed the exposure odds ratio by less than 5%.

We also examined the following three characteristics of day-care exposure to assess their association with respiratory illness: number of other children in the day-care setting, number of hours per week currently in day care, and length of time previously in day care. To simplify the analysis of these factors, we eliminated from the exposed group the children who were currently attending more than one day-care facility or who had switched day-care facilities. Multivariate logistic models incorporating these additional variables were developed from the final exposure models already described.

To take into account the complex survey design, we used RtiLogit, a program that incorporates the design effect into the variance estimates of the logistic parameters, to run the final logistic models.

### Illness in Families

The rates of respiratory illness in the families of exposed children and the families of unexposed children were also examined. Families were classified as exposed if a child (in any age group) attended day care; they were classified as unexposed if their children did not attend day care. Again, multivariate models were developed, as described earlier.

**TABLE 2.** Demographic Characteristics of Children Exposed (Exp) and Children Unexposed (Unexp) to Day Care by Age Group

Characteristic	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp (n = 192)	Unexp (n = 351)	Exp (n = 302)	Unexp (n = 383)	Exp (n = 463)	Unexp (n = 446)
Mean age, mo	11.0	9.0	27.0	26.8	48.4	47.1
Race/ethnicity, %						
White	77.2	74.6	82.2	76.5	72.3	73.3
Black	7.8	8.3	9.6	9.1	14.6	9.0
Hispanic	6.2	11.7	2.6	7.6	6.0	9.9
Other/unknown	8.8	5.4	5.6	6.8	7.1	7.8
Maternal education, %						
<High school	6.4	14.6	7.1	13.7	6.7	10.9
High school	42.3	43.9	40.2	43.3	39.2	52.4
Some college	24.3	24.5	26.0	22.5	26.2	21.4
College degree	27.0	17.0	26.7	20.5	28.0	15.3
Income (in thousands), %						
<\$20	24.4	34.8	23.1	32.1	23.2	35.7
\$20-35	32.6	33.6	33.3	36.6	30.1	34.8
>\$35	38.9	25.6	38.6	26.1	40.6	22.4
Unknown	4.2	6.0	5.0	5.2	6.0	7.2
Region, %						
Northeast	16.6	25.9	19.8	26.9	19.6	19.5
South	37.8	23.1	34.0	25.9	36.8	24.9
North Central	25.9	28.5	26.1	25.3	26.2	30.5
West	19.7	22.5	20.1	21.9	17.4	25.1
Siblings <18, %						
None	39.6	27.9	40.7	23.0	25.9	13.5
Older	60.4	72.1	52.0	64.5	55.3	64.3
Younger only	0	0	7.3	12.5	18.8	22.2

#### Attributable Risk

The attributable risk in the exposed (ARE) estimates the percentage of cases of illness in exposed children that is attributable to the exposure (day care); the population attributable risk (PAR) measures the percentage of the total cases of illness in exposed children and unexposed children that is attributable to the exposure.

For each age group the ARE and the PAR were calculated by using the following formulas:

$$ARE = (I_E - I_U)/I_E$$

$$PAR = P_E(I_E - I_U)/I$$

where  $I$  is the 2-week age-specific incidence of respiratory illness in the total population and  $P_E$  is the proportion of the total population exposed to day care. Because this study excluded children exposed 1 to 10 hours per week, we assumed in estimating  $I$  that the incidence in this group was similar to the incidence in the unexposed group.  $I_E$  represents the estimated incidence of respiratory illness in the exposed population;  $I_U$  is the estimated incidence in a demographically similar unexposed population (ie, adjusted for income, race, and presence of siblings). Logistic regression models were used to calculate these incidence rates.

#### Selected Infectious Diseases in Past Year

Included in the questionnaire were questions about the occurrence in the past year of overnight hospitalizations and 15 specific infectious diseases. Because the exposures and the ages of subjects were different, these analyses were done on a person-year basis. Rates were standardized for region, income, and presence of siblings. Statistical significance was assessed by using the method of Breslow and Day to compare standardized mortality ratios.

#### RESULTS

##### Demographic Characteristics

Comparing the demographic characteristics of the exposed and the unexposed cohorts in each age group revealed that the unexposed tended to have lower levels of maternal education and household income and were more likely to be of Hispanic ancestry (Table 2). Unexposed children were also more likely to have siblings than were exposed children and less likely to live in the South. These and other differences between exposed and unexposed cohorts were considered and, where appropriate, adjusted for in subsequent multiple logistic analyses.



### Characteristics of Day-care Exposure

Table 3 displays various characteristics of day-care exposure. As required by the definition of day-care exposure, all children were enrolled for at least 10 hours per week. Approximately 50% of children in each age group were in day care for 40 or more hours per week (mean time in each age group: 35, 34, and 33 hours per week, respectively). Prior time in day care increased as age increased; almost half (47%) of the children in group 3 had been enrolled in day care for at least 18 months. The percentage of exposed children in small child-care arrangements (6 or fewer children) decreased with age, ranging from 70% of children in group 1 to only 31% of children in group 3.

### Antecedent Illnesses and Events

During the 2 weeks before the interview, the children in all three age groups exposed to day care were more likely to have had a respiratory illness than those not exposed to day care. Furthermore, in each group of children with a respiratory illness, a higher percentage of exposed than unexposed children reported two or more respiratory symptoms (ie, cough, fever, runny nose, sore throat, earache), received antibiotics, and consulted or visited a health care provider (Table 4).

Multiple logistic regression analyses demonstrated that the overall odds ratio for respiratory illness associated with day-care exposure was 1.6 (95% confidence interval [CI], 1.1 to 2.4) for children in group 1 and 1.3 (95% CI, 0.95 to 1.8) for children in group 3 (Table 5). Among those in group 2, the presence of siblings significantly reduced the odds ratio for day-care exposure. Further analysis in this age group of the effect of siblings demonstrated that the day-care odds ratio for children

with younger siblings only was similar to that for children with no siblings and that the aggregate odds ratio for these children was significantly elevated (3.4, 95% CI, 2.0 to 6.0). In contrast, the odds ratio for children with older siblings was significantly lower than above and not significantly different from 1. In the other age groups the odds ratio was not significantly affected by the presence of siblings.

Multiple logistic analysis concerning children without siblings (thereby allowing direct comparisons of age groups) demonstrated day-care odds ratios of 1.8, 3.7, and 1.5 for age groups 1, 2, and 3, respectively. The odds ratio for children in group 2 was 2.0-fold higher (95% CI, 0.74 to 5.4) than that for children in group 1 and 2.4-fold higher (95% CI, 0.93 to 6.4) than that for children in group 3.

To further assess the possible independent risk of respiratory illness due to exposure to older siblings, we also calculated odds ratios of respiratory illness associated with other siblings (Table 5). In group 1, the odds ratio (1.7) was significantly elevated. In group 3, the odds ratio was significantly below 1, suggesting that in this age group the risk of respiratory illness was lower in children with older siblings than in those without. In both these groups, no interaction with day-care exposure was observed. For children in group 2, the older-sibling odds ratio was affected by day-care status. For those not in day care, the odds ratio for older siblings was significantly elevated; however, among those in day care the odds ratio was less than 1.

### Characteristics of Day-care Exposure Related to the Risk of Illness

Using exposure to a single day-care facility, we included 87%, 80%, and 72% of exposed children in age groups 1, 2, and 3, respectively, in the analysis. For each age group, the odds ratio of respiratory illness associated with current day-care exposure did not differ significantly between part-time (<40 hours/week) and full-time care.

For each age group the Figure displays how the duration of past day-care exposure influences the odds ratio of respiratory illness associated with current day-care exposure. Within each age group, the protective effect of longer enrollment in day care was statistically significant. In group 1 the odds ratio of respiratory illness for those exposed less than 9 months was 2.3 times as great as the odds ratio for those exposed greater than 9 months. Similarly, for those in age groups 2 and 3, exposure to day care for less than 9 months was associated with a 2.1- and 2.2-fold-greater odds ratio, respectively, than was exposure for 18 to 27 months. As

TABLE 3. Characteristics of Day-care Exposure\*

Characteristic	Age Group		
	6 wk-17 mo	18-35 mo	36-59 mo
Size of day-care facility			
2-6	133 (70)	167 (56)	141 (31)
7+	58 (30)	133 (44)	317 (69)
Prior time in day care			
<9 mo	116 (67)	94 (32)	154 (34)
9-18 mo	57 (33)	84 (29)	86 (19)
18-27 mo		88 (30)	88 (19)
>27 mo		27 (9)	128 (28)
Hours/wk in day care			
≥10-19	29 (15)	38 (13)	109 (24)
20-39	60 (32)	115 (38)	141 (31)
≥40	101 (53)	148 (49)	207 (45)

\* Results are given as number (%) of children.

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**TABLE 4.** Illness and Events Within 2 Weeks Before Interview: Children Exposed (Exp) and Children Unexposed (Unexp) to Day Care, by Age Group\*

Illness/Event	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp	Unexp	Exp	Unexp	Exp	Unexp
All Children						
Respiratory illness	34.2	26.5	37.6	29.5	25.8	21.5
Children With Respiratory Illness						
≥2 symptoms	78.8	73.1	80.7	70.8	82.5	71.9
Symptoms for ≥2 days	98.3	100.0	95.2	92.6	96.4	92.9
Consulted/visited health care provider	66.1	60.4	49.5	43.4	55.3	39.1
Received antibiotics	40.7	31.1	29.9	25.0	35.0	19.8

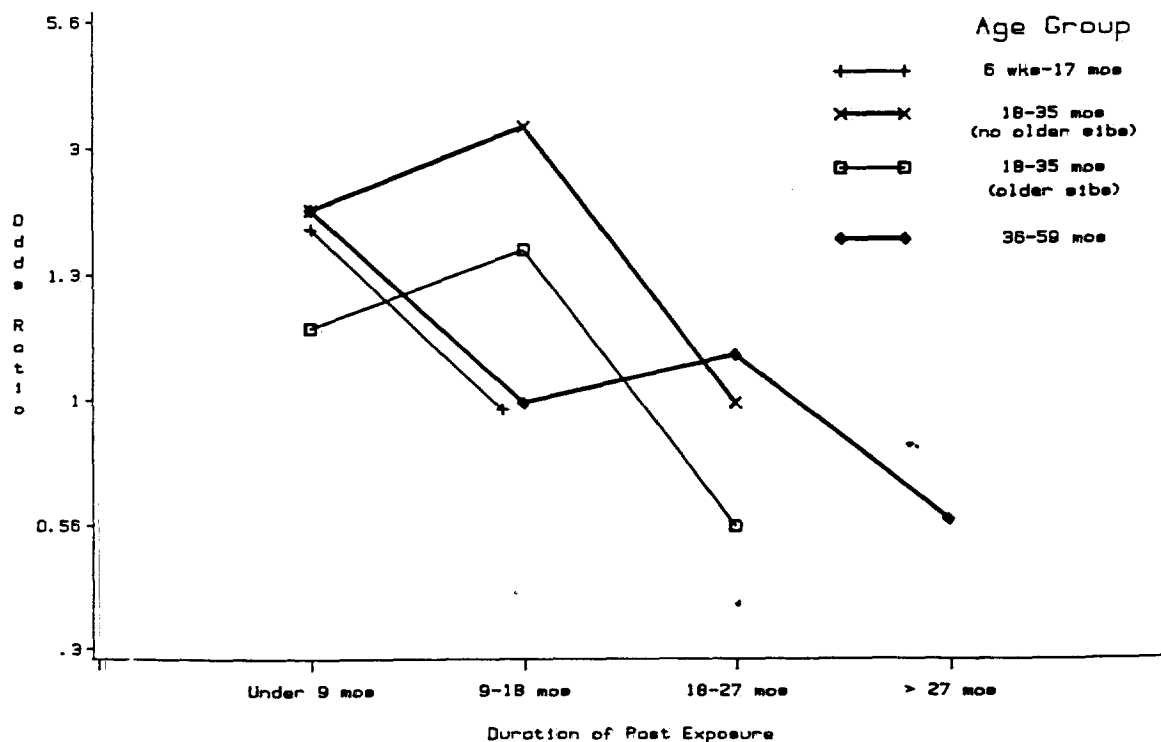
\* Results are percentages.

**TABLE 5.** Odds Ratios, by Age Group, for Respiratory Illness Associated With Day-care Exposure and With Having an Older Sibling\*

OR	Age Group		
	6 wk-17 mo	18-35 mo	36-59 mo
Daycare OR (95% CI)			
Older sibs		1.0 (0.65-1.6)	
No older sibs		3.4 (2.0-6.0)	
Aggregate†	1.6 (1.1-2.4)		1.3 (0.95-1.8)
Older sibling OR (95% CI)			
Day care		0.62 (0.38-1.0)	
No day care		2.1 (1.2-3.7)	
Aggregate†	1.7 (1.1-2.6)		0.60 (0.41-0.88)

\* OR, odds ratio; CI, confidence interval.

† Aggregate odds ratio used when no significant interaction observed.



**Figure.** Odds ratios of respiratory illness associated with day-care exposure by duration of past exposure and age group.

seen in the Figure, odds ratios well below 1 were observed in several situations. The odds ratio for children in group 3 who had been in day care for more than 27 months was 0.58 (95% CI, 0.23 to 1.1); the odds ratio for children in group 2 who had been in day care for more than 18 months and who had older siblings was 0.56 (95% CI, 0.22 to 1.03).

In each age group the odds ratio associated with larger (more than six children) vs smaller day-care facilities was elevated. This effect was greatest, and statistically significant, in group 2 (odds ratio = 2.2; 95% CI, 1.2 to 3.7). The odds ratios for large vs small centers were 1.6 and 1.4, respectively, for groups 1 and 3.

### Illness in Family Members

Respiratory illness in family members 5 years of age or older was highly correlated with the occurrence of respiratory illness in family members younger than 5 years of age in exposed and in unexposed families. Thirty-one percent (72/230) of exposed families with ill children younger than 5 years of age also reported a respiratory illness in a family 5 years of age or older compared with 12% (73/608) of exposed families with no ill children younger than 5 years of age; the comparable percentages for unexposed families were 36% (71/199) and 12% (90/744). Thirty-eight exposed families (4.5%), compared with 34 (3.6%) unexposed families, reported a respiratory illness in a family member 5 years of age or older that was preceded in the 2 weeks before interview by the onset of a respiratory illness in a family member younger than 5 years of age.

The results of the logistic model demonstrated that families that reported a respiratory illness in a member 5 years of age or older were 1.18 times as likely to have children in day care as were the families that reported no illness in a member 5 years of age or older (95% CI, 0.93 to 1.50).

### Attributable Risk

The ARE for respiratory illness was higher for groups 1 and 2 (28% and 33%) than for group 3 (18%). The PARs for the three age groups were 7.1%, 11.7%, and 7.7%, respectively. The similarity of the PARs in groups 1 and 3, despite the difference in AREs, reflects that a higher proportion of children in group 3 than in group 1 were exposed to day care.

### Infectious Illnesses in the Past Year

We compared the incidence rates of certain infectious illnesses in the year preceding the interview

by age and exposure status (Table 6). In each age group, the exposed incidence rate for chickenpox exceeded the unexposed rate; this difference was statistically significant for groups 1 and 3. No significant differences were observed in the incidence rates of selected other diseases listed in the table nor for respiratory-tract-related hospitalizations.

Because chicken pox was the only disease with enough cases for subset analyses, we used it to examine the effect of older siblings and the size of the day-care facility, two factors that are important for day-care-associated respiratory illness. Similar trends were observed. In groups 1 and 3 relative risks of more than 2 for day-care exposure were observed for the children with and children without older siblings. In group 2, however, only those without older siblings had an elevated relative risk (2.3); those with older siblings had a relative risk of 1.0. In addition, in each group, the risk for large centers exceeded that for small centers; relative risks of 1.6, 1.5, and 1.4 were observed for groups 1 through 3, respectively.

### DISCUSSION

The results of this nationwide study are consistent with observations from a number of studies conducted in smaller populations using a variety of methods, which suggest that day-care attendance is associated with an increased risk of respiratory illnesses in preschool-aged children.<sup>3-7</sup> In addition,

**TABLE 6.** Incidence Rates per 100 Child Years of Reported Infectious Illnesses in Past Year, by Age Group and Day-care Exposure\*

Disease	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp	Unexp	Exp	Unexp	Exp	Unexp
Chickenpox	9.5 <sup>  </sup>	3.5	11.2	8.2	19.5	8.3
Diarrhea lasting >1 wk	5.8	4.4	4.0	5.4	0.8	1.7
Vaccine-preventable diseases <sup>†</sup>	0.5	0.8	1.1	0.7	0.7	0.3
Other diseases <sup>‡</sup>	3.1	1.5	3.4	1.7	4.9	4.2
Respiratory-related hospitalizations <sup>§</sup>	3.0 <sup>  </sup>	3.1	2.1	2.0	0.3	0.0

\* Exp, children exposed to day care; Unexp, children unexposed to day care.

<sup>†</sup> Includes measles, mumps, rubella, diphtheria, and pertussis (no cases of mumps or diphtheria reported).

<sup>‡</sup> Includes mononucleosis, scarlet fever, scabies, lice, hepatitis, meningitis, giardiasis, and *Haemophilus influenzae* (no cases of hepatitis or meningitis reported).

<sup>§</sup> Includes pneumonia, influenza, bronchitis, asthma, and respiratory condition (unspecified).

<sup>||</sup> Significant difference between exposed and unexposed rate.

this study allowed examination of a number of issues, including the effect of prolonged exposure to day care and to older siblings, which had not been assessed in earlier studies. This study illustrates the complexity of this day-care-associated risk and the fact that a number of factors, including age of the child, presence of older siblings in the home, duration of prior day care, exposure, and size of the day-care facility may affect the risk of such illnesses.

The risk of respiratory illness associated with day-care attendance increased for children in all three age groups, although it was statistically significant only for (all) children in the youngest age group and children without older siblings in the 18-through 35-month age group. The highest risk was observed in this latter group (odds ratio = 3.4). The risk of respiratory illness in children aged 18 through 35 months with older siblings was not affected by day-care attendance; however, these children did have an excess risk of respiratory illness when compared with children who had neither older siblings nor day-care exposure. This group may have no day-care-related risk of respiratory illness because older siblings and day care pose similar and competing risks in this age group.

Although authors have speculated about differing day-care-related risks among children of different ages, earlier studies have not examined the risk of respiratory illness among children of different ages, and many have not included children older than 36 months of age.

Infants and toddlers in day care have also been shown to have increased risks of other illnesses, particularly diarrhea.<sup>8</sup> Inasmuch as many of the modes of transmission of agents commonly responsible for diarrheal and respiratory illnesses are believed to be similar—including child-to-child contact and fomites or shared objects, which are frequently mouthed by infants and toddlers—the increased risk of both types of illness is not unexpected. The higher day-care-associated rate of respiratory illness in children aged 18 through 35 months compared with younger and older children may be related to an increased frequency of such practices in this age group. Additionally, the lower day-care-associated risk (and absolute rates) of respiratory illness in children aged 36 through 59 months may be related to the acquisition of relative immunity to common respiratory agents. Although this study was not designed to assess all possible differences among children of different ages, it does illustrate the importance of considering age when examining day-care-related risk of respiratory illness.

Although there has been considerable speculation about the impact of early and long-term enrollment

in day care on the risk of various illnesses, especially respiratory illnesses, this is the first study to assess this factor using large cohorts of children who have been in day care for different lengths of time. Our results suggest that among children attending a single facility (87%, 80%, and 72% in age groups 1, 2, and 3, respectively), longer exposure was associated with a decreased risk of respiratory illness. This seemed to be true regardless of the size of the facility and was apparent in each age group. Among children aged 36 through 59 months, those who had been in day care for 27 or more months had a lower risk than those unexposed to day care (odds ratio = 0.5), suggesting that prolonged exposure to day care may lead to a reduced risk of respiratory illness among older preschool children. It is possible that this reduced risk of respiratory illness extends into the school-aged years and results in decreased absenteeism during this period. On the other hand, the increased rate of respiratory infections during the earlier years may be related to an increased risk of otitis media and associated complications, an issue our study did not address.<sup>9-11</sup>

This study suggests that the presence of older siblings in the home, as well as day-care attendance, has an important, and perhaps similar, impact on the risk of respiratory illness in children younger than 5 years of age. Among children aged 6 weeks through 17 months, the odds ratios associated with older siblings and with day care were similarly elevated. Among those 18 through 35 months of age, the odds ratio associated with older siblings among those not in day care was elevated but of smaller magnitude than the odds ratio for day care among those without older siblings. However, among children 36 through 59 months of age, the odds ratio associated with older siblings was less than 1 (odds ratio = 0.54,  $P < .05$ ), suggesting a protective effect. Thus, prolonged exposure to older siblings seemed to reduce the risk of respiratory illness.

Although risk of respiratory illness increased in association with day care, the size of the day-care facility significantly affected this risk only among those children 18 through 35 months of age; attendance at a larger facility (more than six children) was associated with a significantly increased risk of respiratory illness when compared with smaller facilities (two to six children, odds ratio = 2.2). Although there is considerable evidence that larger day-care facilities are associated with an increased risk of certain illnesses, including diarrhea and disease caused by *H influenzae*,<sup>8,12</sup> studies concerning the importance of the size of the facility have been less conclusive and have not attempted to evaluate this risk among children of different ages.

Wald et al recently reported that children younger than 18 months of age in smaller day-care facilities (two to six children) had an intermediate risk of respiratory illness between home care and larger day-care facilities; in our study, however, the difference between small and larger settings was not statistically significant for children younger than 18 months of age.<sup>4</sup> Strangert, too, found no evidence that increasing the number of contacts to more than four to six children increased the risk of respiratory disease among children younger than 2 years of age.<sup>5</sup>

Although we observed no differences in the risk of a number of illnesses, including lower respiratory tract illness, meningitis, and measles, we had too few cases to adequately assess possible differences in the risk of these illnesses with respect to day-care attendance. However, the increased risk of chickenpox was statistically significant for those attending day care. Furthermore, chickenpox was similar to respiratory illness in terms of the influence of older siblings and the size of the day-care facility.

A major distinction of this study is that the participants represent a cross-section of day-care attendees and nonattendees in the United States. However, a number of limitations should be considered in assessing the results. The study primarily focused on illnesses occurring in the 2 weeks before the telephone interviews, which were conducted from March 17th through June 12th, rather than during the peak period of respiratory illnesses (winter months of December through March). Caution should be used in extrapolating these results to other seasons of the year.

Additional concerns include the possibility that the parents of children attending day-care centers may be more likely to report minor symptoms as illnesses because of a preconception that such facilities are associated with an increased risk of illness. However, most of the illnesses reported by parents involved two or more respiratory symptoms that lasted 2 or more days, and many involved antibiotic therapy; furthermore, these indices of severity were reported more frequently for exposed children than for unexposed children.

That this study consisted of a nationwide representative sample of children enrolled in day care makes the assessment of attributable risk potentially meaningful from a public health perspective. Our estimates that approximately 20% to 30% of respiratory illnesses among those attending day care can be attributed to day care and that 7% to 12% of all respiratory illnesses in children younger than 5 years of age occurring in the United States during the study period may have resulted from day-care attendance are similar to those reported

for children (all <36 months) in a study conducted in metropolitan Atlanta from mid-July to mid-September.<sup>3</sup> The present study also suggests that small, compared with larger, day-care settings, specifically for children 18 through 35 months of age, are associated with a reduced risk of respiratory illness. In addition, the study also illustrates that one possible result of early day-care enrollment may be a reduced risk of respiratory illnesses among older preschool children. Further studies, including studies prospectively observing large cohorts of children in various types of day-care settings, would help determine whether a reduced rate of respiratory illness extends into the school-aged years.

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Dales, R.E., Zwanenburg, H., Burnett, R., and Franklin, C.A., "Respiratory Health Effects of Home Dampness and Molds Among Canadian Children," American Journal of Epidemiology 134: 196-203, 1991.

The authors report that "prevalences of all respiratory symptoms were consistently higher in homes with reported molds or dampness; i.e., adjusted odds ratios ranged from 1.32 (95% confidence interval 1.06-1.39) for bronchitis to 1.89 (95% confidence interval 1.58-2.26) for cough." They suggest that "the prevalence of home dampness or molds, 37.8%, indicates that it is an important public health issue." The reported associations were independent of the age and sex of the child, the number of household smokers, the presence of gas stoves, and the region of residence in Canada.

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## Respiratory Health Effects of Home Dampness and Molds among Canadian Children

Robert E. Dales,<sup>1,2</sup> Harry Zwanenburg,<sup>1</sup> Richard Burnett,<sup>1</sup> and Claire A. Franklin<sup>1</sup>

In 1988, the authors conducted a questionnaire-based study on the health effects of the indoor environment in 30 Canadian communities. This paper focuses on the association between the respiratory health of young children and home dampness and molds. A total of 17,962 parents or guardians of schoolchildren received a questionnaire, and 14,948 (83.2%) questionnaires were returned. Children living in mobile homes, tents, and boats were excluded as were those with cystic fibrosis, leaving 13,495 children included in the study group. The housing stock was distributed as follows: 81% were one-family detached homes, 6% were one-family attached homes, and 13% were buildings for two or more families. Molds were reported in 32.4%, flooding in 24.1%, and moisture in 14.1% of the homes. Prevalences of all respiratory symptoms were consistently higher in homes with reported molds or dampness; i.e., adjusted odds ratios ranged from 1.32 (95% confidence interval 1.06–1.39) for bronchitis to 1.89 (95% confidence interval 1.58–2.26) for cough. The prevalence of home dampness or molds, 37.8%, indicates that it is an important public health issue. Further studies are required to elucidate the pathogenesis. *Am J Epidemiol* 1991;134:196–203.

environment; environmental pollution; humidity; respiratory tract diseases

Indoor air quality is understandably an important health issue, since North Americans spend the majority of their time indoors (1). This is especially important in Canada where homes tend to be well insulated because of the cold climate and consequently may have reduced fresh air exchange (2).

Home dampness with resulting mold growth may occasionally cause an immedi-

ate hypersensitivity reaction, hypersensitivity pneumonitis, or humidifier fever (3–5). The association between the occurrence of molds and dampness in the indoor environment with the prevalence of nonspecific respiratory symptoms in young children is of particular interest at present (6–8).

In a case study of "problem" houses in various parts of Canada, about 20 percent were found to have undesirably high internal moisture strength values, >2 kg of H<sub>2</sub>O/hour (9). However, the burden of illness among Canadian children associated with living in homes with dampness or molds is unknown. Therefore, in 1988 we conducted a large questionnaire-based study of the health effects of the indoor environment in Canadian homes. Questionnaires were distributed to the parents of children in kindergarten through grade two. The health effects of home dampness among the adult respondents have been reported elsewhere (10). This paper focuses on the association be-

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tween the respiratory health of young children and the presence of home dampness and molds.

## MATERIALS AND METHODS

### Study sites

Thirty communities were selected for the present study based on several criteria, including the following: similar distributions of children 5–8 years old and family income levels based on information from the 1986 Census, no major local sources of industrial air pollution verified by site visits, and knowledge of approximate exposure levels to long-range transported air pollution (ozone and sulfates). Sets of five communities with similar exposure to sulfate were clustered together into six regions (figure 1). Two regions, the interior of British Colum-

bia and Saskatchewan, had relatively low levels of estimated average annual sulfate ( $\sim 1 \mu\text{g}/\text{m}^3$ ); southwestern Ontario had the highest levels ( $5.0\text{--}6.0 \mu\text{g}/\text{m}^3$ ); and the Muskoka area of Ontario, Quebec, and the maritime provinces had intermediate levels. The association between respiratory health and long-range transported air pollution will be reported elsewhere.

### Study population

The target population consisted of children in kindergarten and grades one and two, who were also between the ages of 5 and 8 years old. Questionnaires, to be completed by the parent or guardian most familiar with the child's health, were distributed via the schools during the period from March 15 to April 8, 1988.

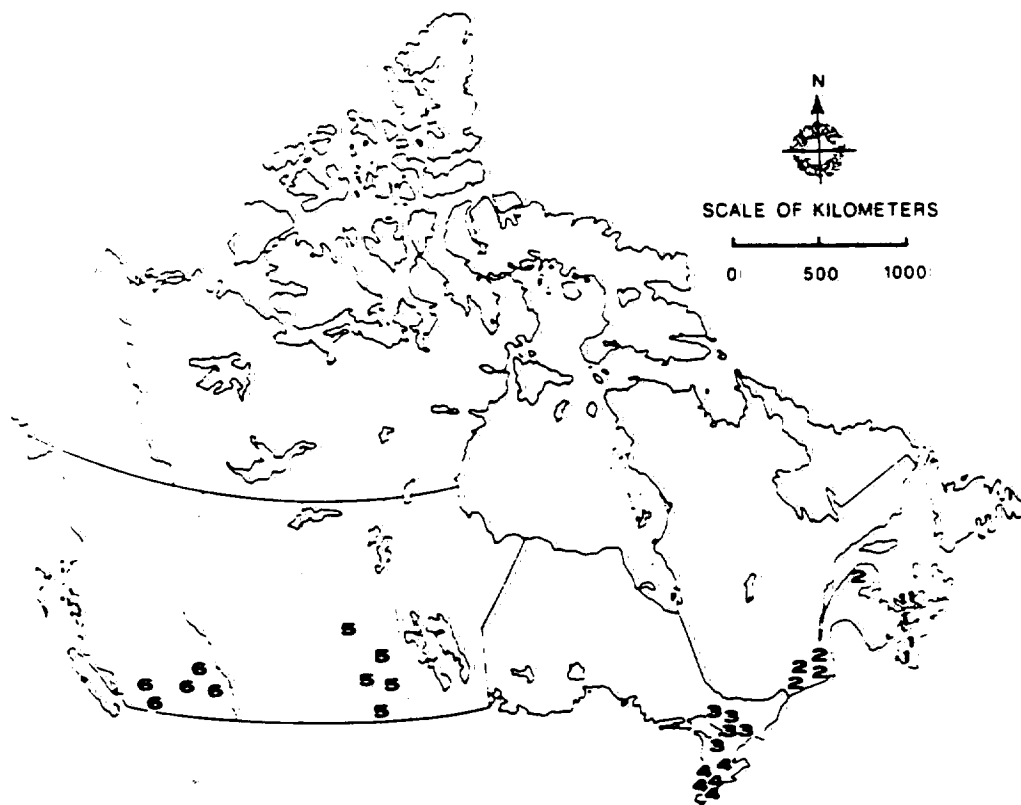


FIGURE 1. Map of Canada showing the location of the six selected regions. They are the maritime provinces (1), Quebec (2), Muskoka area of Ontario (3), southwestern Ontario (4), Saskatchewan (5), and British Columbia (6). Five communities were studied within each region.

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People living in mobile homes or trailers, boats, tents, and vans were excluded from the present analyses, because the indoor environments were considered to be potentially different from the common types of residence buildings. Children whose parents answered "yes" to the question, "Has a doctor ever said that this child had cystic fibrosis?" were also excluded.

### The questionnaire

Questions used in this study were taken or modified for our purposes from four previously used instruments: the American Thoracic Society-Division of Lung Disease Respiratory Symptom Questionnaire (11), the Environmental Inventory Questionnaire (12), the questionnaire used by the Harvard School of Public Health for the Harvard Six Cities Study (13), and the questionnaire used by Health and Welfare Canada for a community-based study of children's health (14).

Since no consensus existed as to which questions best indicated the burden of exposure to household molds, we, as other investigators have done, developed questions concerning visible mold growth and humid (micro)environments that promote mold growth (15). This was done through extensive consultation with a mycologist, microbiologist, and toxicologist who have previously reported on indoor air fungi (2).

From our composite questionnaire, the *primary exposure variables* used to indicate the presence of dampness and molds were defined as follows: *mold sites*, number of sites (basement, shower area, elsewhere in home) with visible mold or mildew in the past year; *moisture*, appearance of wet or damp spots, excluding the basement in the past year; *flooding*, appearance of flooding, water damage, or leaks in the basement in the past year; and *dampness/mold*, any one of the above three variables being positive (mold sites, moisture, or flooding).

The *primary health outcomes* were defined as follows: *persistent cough*, a cough present for 3 months of the year or more, apart from colds; *persistent wheeze*, wheez-

ing apart from colds, wheezing accompanied by dyspnea, wheezing present most days and nights, or wheezing after exercise; *wheeze with dyspnea*, wheezing accompanied by dyspnea; *current asthma*, asthma currently present and reported to be confirmed by a physician; *chest illness*, a chest illness requiring the child to stay at home for 3 days or more; *upper respiratory symptoms*, nose irritation, runny and stuffy nose, sneezing, or throat irritation occurring on three or more separate occasions in the last 3 months; *nonrespiratory symptoms*, any one of headaches, muscle aches, fever and chills, nausea, vomiting, or diarrhea occurring on three or more separate occasions in the last 3 months; and *eye irritation*, itchy eyes experienced on three or more separate occasions in the last 3 months.

Information was also collected on factors that could influence the primary relation of interest. These covariables were defined as age, sex, race (Caucasian, other), highest level of education of either parent or guardian (completed at least some postsecondary education, other), number of household smokers (none, any), cooking fuel (gas, other), hobbies (presence or absence of woodworking, glassblowing, painting, other), sex of respondent, and region of residence. Analyses were also stratified by the report of a physician-confirmed allergy to mold (present, absent) or dust (present, absent) occurring in the past year.

To investigate a possible over- or under-reporting bias, we defined another variable "accidents or illnesses," which was a major illness or accident unrelated to the chest, occurring in the past year, that restricted his or her activity for at least 1 week.

### Statistical analysis

First, the crude odds ratios of the associations between health outcomes and home dampness were calculated. Odds ratios were tested for differences from unity by the  $\chi^2$  test (PROC FREQ, SAS version 5) (16). Symptom prevalences were stratified by the presence or absence of home dampness/mold both to demonstrate the proportion of

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people affected and to help interpret the odds ratios that deviate more from the null than prevalence ratios, particularly with high prevalences. Multiple logistic regression, using the maximum likelihood method, was applied to adjust for confounders and to improve precision. The study population was stratified by the presence or absence of mold and dust allergy to indicate whether or not allergic mechanisms influenced the relation. The data were also stratified by the presence or absence of "accidents or illnesses" to assess the influence of reporting bias. Differences in the odds ratios across strata were examined by the Breslow-Day test for homogeneity of odds ratios (PROC FREQ, SAS version 5) (16). The strength of association among the health responses was tested by Kendall's tau.

## RESULTS

A total of 17,962 parents or guardians received a questionnaire, and 14,948 (83.2 percent) questionnaires were returned. Data on 13,495 children were available for analysis after excluding those who were less than 5 or greater than 8 years of age ( $n = 323$ ); those with cystic fibrosis ( $n = 17$ ); and those who lived in mobile homes or trailers, tents, or vans ( $n = 547$ ). Subjects with no recorded age ( $n = 475$ ) or housing type ( $n = 131$ ) were also excluded. During the school year, 99.6 percent of the children slept in the home of the respondent (parent/guardian) for five or more nights per week. The housing stock distribution was as follows: 81 percent were one-family detached homes, 6 percent were one-family attached homes, and 13 percent were buildings for two or more families. The reported prevalence of molds was 32.4 percent, moisture was 14.1 percent, and flooding (reported in homes with a basement) was 24.1 percent.

As demonstrated in table 1, children living in homes with reported dampness/mold had age, sex, race, and gas cooking distributions similar (i.e., <2 percent differences) to those living in homes without reported dampness/mold. Parental education was greater in homes with reported dampness/mold: 58

TABLE 1. Host and environmental characteristics: selected Canadian children, 5-8 years old, 1988

Host and environmental characteristics	Dampness/mold*	
	Absent (%)	Present (%)
Child's age (years)		
5	19.0	21.1
6	32.1	31.9
7	33.2	32.5
8	15.6	14.5
Child's sex		
Male	50.5	51.7
Female	49.5	48.3
Child's race		
Caucasian	96.4	96.8
Other	3.6	3.2
Mold allergy		
Yes	2.7	4.9
No	97.3	95.1
Dust allergy		
Yes	5.1	7.6
No	94.9	92.4
Respondent's sex*		
Male	17.8	15.4
Female	82.2	84.6
Parental education*		
High school or less	47.3	41.7
More than high school	52.7	58.3
Household smokers*		
Any	50.5	55.3
None	49.5	44.7
Gas cooking		
Yes	5.1	5.7
No	94.9	94.3
Hobbies*		
Yes	12.4	14.9
No	87.6	85.1

\*  $p < 0.01$ ,  $\chi^2$  test

† For the study group of 13,495 children, values for dampness/mold were available for 12,569; dampness/mold values were absent for 7,814 and present for 4,755 children

percent had postsecondary school education compared with 53 percent in "dry" homes. Household smoking was also more prevalent in damp homes, 55 percent versus 51 percent.

As shown in table 2, the reported prevalences of lower respiratory symptoms/disorders (cough, wheeze, asthma, bronchitis, and chest illness) were approximately 50 percent higher in damp homes. Upper respiratory and nonrespiratory symptoms were increased by 20-25 percent.

Odds ratios for the individual symptoms comprising the "nonrespiratory symptoms"

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variable ranged from 1.33 for vomiting to 1.63 for muscle aches. Crude odds ratios for the associations between health indicators and indicators of home dampness or molds are presented in table 3. Cough appeared to be the symptom with the greatest odds ratio. The presence of two mold sites appeared to be the exposure with the greatest odds ratios. All health indicators were associated ( $p <$

0.05) with all indicators of home dampness or molds; odds ratios ranged from 1.14 for flood and bronchitis to 2.26 for cough and two mold sites. For all of the health indicators, odds ratios were greater for two than one reported mold site, indicating a dose-response relation. It must be pointed out, however, that the consistency observed in the results in table 3 was simply due to neither high correlations among health indicators nor high correlations among all the indicators of dampness or molds. Kendall's tau showed weak correlations, generally less than 0.3, among health indicators. Exceptions were among wheeze, wheeze with dyspnea, and asthma, where correlations were approximately 0.6.

Odds ratios were adjusted for age, sex, race, education of parent/guardian, gas cooking, number of household smokers, hobbies, sex of respondent, and region of residence. Overall, adjusted odds ratios ranged from 1.08 for wheeze with dyspnea and flooding to 2.55 for the association between cough and number of mold sites. The 95 percent confidence interval for the adjusted odds ratios included one only for the associations between flood and the two wheezing syndromes and between flood and asthma. Adjusted odds ratios were very similar to the crude odds ratios. The largest

TABLE 2. Prevalences of health indicators stratified by the presence or absence of dampness/mold: selected Canadian children, 5-8 years old, 1988

Health indicators	Dampness/mold* †	
	Absent (%)	Present (%)
Cough	4.4	7.9
Wheeze	10.9	16.2
Wheeze with dyspnea	5.3	8.3
Asthma	4.0	5.7
Bronchitis	9.9	12.7
Chest illness	9.9	14.3
Upper respiratory symptoms	48.6	59.0
Eye irritation	5.6	8.3
Nonrespiratory symptoms‡	30.7	38.8

\* All differences between dampness/mold are significant at  $p < 0.01$ ,  $\chi^2$  test.

† For the study group of 13,495 children, values for dampness/mold were available for 12,569; dampness/mold values were absent for 7,814 and present for 4,755 children.

‡ Any one of headaches, muscle aches, fever and chills, nausea, vomiting, or diarrhea occurring on at least three separate occasions in the last 3 months.

TABLE 3. Unadjusted odds ratios for the association between health and home dampness/mold: selected Canadian children, 5-8 years old, 1988

Health indicator	Dampness/mold		Flood		Moisture		No. of mold sites			
	OR*	95% CI*	OR	95% CI	OR	95% CI	0 vs. 1		0 vs. 2	
							OR	95% CI	OR	95% CI
Cough	1.89	1.63-2.20	1.38	1.16-1.65	1.91	1.60-2.27	1.61	1.36-1.89	2.26	1.80-2.83
Wheeze	1.58	1.42-1.76	1.25	1.10-1.41	1.74	1.53-1.98	1.42	1.26-1.59	1.73	1.45-2.06
Wheeze with dyspnea	1.61	1.40-1.86	1.24	1.05-1.47	1.68	1.41-1.99	1.56	1.34-1.82	2.00	1.60-2.50
Asthma	1.45	1.23-1.71	1.29	1.06-1.56	1.58	1.29-1.94	1.40	1.16-1.68	1.67	1.27-2.19
Bronchitis	1.32	1.18-1.48	1.14	1.00-1.31	1.49	1.30-1.72	1.25	1.10-1.42	1.46	1.20-1.78
Chest illness	1.52	1.37-1.70	1.50	1.32-1.70	1.47	1.28-1.69	1.54	1.36-1.73	1.81	1.51-2.17
Upper respiratory symptoms	1.46	1.36-1.57	1.26	1.16-1.38	1.52	1.38-1.68	1.36	1.25-1.47	1.74	1.52-2.00
Eye irritation	1.53	1.33-1.76	1.42	1.21-1.66	1.60	1.35-1.90	1.42	1.21-1.65	1.74	1.39-2.19
Nonrespiratory symptoms†	1.43	1.33-1.55	1.25	1.14-1.37	1.45	1.31-1.60	1.28	1.18-1.39	1.72	1.50-1.96

\* OR, odds ratio; 95% CI, 95% confidence interval.

† Any one of headaches, muscle aches, fever and chills, nausea, vomiting, or diarrhea occurring on at least three separate occasions in the last 3 months.

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differences were as follows. Between eye irritation and moisture, the crude and adjusted odds ratios were 1.60 and 1.90, respectively; between cough and two mold sites, the crude and adjusted odds ratios were 2.26 and 2.55; and between eye irritation and two mold sites, the crude and adjusted odds ratios were 1.74 and 1.52. All other differences were less than 0.2.

The associations between respiratory health indicators and home dampness/mold were slightly weaker in the presence versus the absence of mold or dust allergy. However, differences in odds ratios between strata were significant at  $p < 0.05$  only for wheezing, wheezing with dyspnea, and asthma (table 4).

The associations between symptoms and dampness/mold were present within all regions except for British Columbia where the unadjusted odds ratios were 1.05 for wheeze, 0.94 for dyspnea with wheeze, and 0.64 for asthma. Stratification by the variable representing accidents or illnesses not of the chest (indicating reporting bias) did not remove the associations shown in table 3. To ensure that responses to this question were not related to the primary outcome variables of interest, we included only the following reported problems: poison ivy, appendicitis, kidney disorders, surgery, gum disorders, pregnancy, trauma, and pituitary tumors.

## DISCUSSION

We found that the reported presence of indoor molds and dampness may cause adverse health effects in Canadian children. Consistent with a causal relation were the following observations. 1) A dose-response gradient was demonstrated between the number of mold sites and health outcomes with a maximum odds ratio reaching 2.55 for cough and the presence of two mold sites. 2) The observed relation was independent of the age and sex of the child, the number of household smokers, the presence of gas stoves, and the region of residence in Canada. 3) Respondents were essentially "blinded" to the hypothesis tested. The questionnaire did not focus on home dampness exclusively, and it is not generally known that home dampness and molds cause adverse health effects. 4) It is unlikely that general over- or underreporting biased the study because stratifying by the question used to indicate reporting bias did not erase the observed relation. However, this cannot be excluded, as the question used is at best a crude indicator of reporting bias. 5) Parents of "symptomatic" children, searching for etiologic factors, may be more aware of indoor air problems than parents of asymptomatic children. This could also lead to an observed association between symptoms and

TABLE 4. Odds ratios for the association between health indicators and dampness/mold stratified by reported mold allergy: selected Canadian children, 5-8 years old, 1988

Health indicator	Mold allergy <sup>a</sup>		Dust allergy <sup>†</sup>	
	Absent	Present	Absent	Present
Cough	1.74‡	1.39	1.69‡	1.60‡
Wheeze	1.59‡,§	0.78	1.56‡	0.98§
Wheeze with dyspnea	1.68‡,§	0.68	1.62‡	0.94§
Asthma	1.51‡,§	0.64‡	1.38‡	1.04
Bronchitis	1.28‡	1.25	1.28‡	1.25
Chest illness	1.49‡	1.04	1.45‡	1.30
Upper respiratory symptoms	1.43‡	1.75‡	1.39‡	1.91‡
Nonrespiratory symptoms	1.41‡	1.19	1.40‡	1.36‡
Eye irritation	1.42‡	1.41‡	1.33‡	1.69‡

<sup>a</sup> For the study group of 13,495 children, values for mold allergy were available for 12,947; mold allergy values were absent for 12,423 and present for 524 children.

<sup>†</sup> For the study group of 13,495 children, values for dust allergy were available for 12,958; dust allergy values were absent for 12,173 and present for 785 children.

‡ Odds ratio significantly different from unity at the 5% level.

§ Breslow-Day test for homogeneity of odds ratios between the presence or absence of mold allergy ( $p < 0.05$ ).

|| Any one of headaches, muscle aches, fever and chills, nausea, vomiting, or diarrhea occurring on at least three separate occasions in the last 3 months.

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dampness/mold. The result presented in table 4 argues against this scenario. Among children with known dust and mold allergies, the association between symptoms and exposures was no stronger than that among children without these known allergies. Finally, our Canadian findings are consistent with those in other countries as discussed below.

Dampness or mold, determined by either questionnaire or building inspection, in the homes of Edinburgh school children has been strongly associated with respiratory symptoms in several studies (6, 17-19). For example, in one study the crude odds ratio for the presence of any respiratory symptom was 3.7,  $p < 0.01$  (19). A small questionnaire study of 185 homes in The Netherlands also reported crude odds ratios of 2-3 for the associations between respiratory symptoms and home dampness (7). A larger questionnaire study of 4,990 Swedish children, whose parents were nonsmokers, found dampness to be associated with cough as indicated by an odds ratio of 1.9,  $p < 0.05$  (20). Another large study of 4,625 US children reported odds ratios similar to ours of 1.2-2.2 between respiratory symptoms and home dampness or molds after adjusting for maternal smoking, age, sex, city of residence, and parental education (8). Thus, the Canadian experience is similar to those of other countries despite differences in questionnaires, languages, climate, and housing.

Although there are several facts supporting the argument for causality, both the exposure and outcome variables were based entirely on questionnaire reporting. This crude subjective measure of molds would be expected to result in misclassification of exposure and, if random, to reduce the observed effect size. Previous studies have demonstrated that reported molds and dampness have some validity as measures of mold concentrations and dampness in homes, although correlations were weak (7, 20). Currently it is not possible to test the validity of questionnaire reports as an indicator of mold-related pathogenic agents. The nature of these agents is unknown and, therefore, cannot be directly measured for

use as a criterion (or gold standard). Concentrations of mold measured as colony-forming units will not include the nonviable but potentially allergenic portion (21). Large temporal variations in airborne mold concentrations occur, for example, from the activities of occupants (2, 21). Thus, the often used "grab samples" may not well represent average or peak exposures. Furthermore, total spore counts or colony-forming units may poorly reflect the presence of small proportions of certain species that may have important health effects (2). Heterogeneity also exists within a given species: mycotoxin production is related to both the species and its local environmental conditions (2). Furthermore, dampness indicates inadequate home ventilation and perhaps increased levels of several contaminants. The observed prevalence of any dampness/mold in the present study, 38 percent, probably overestimates the prevalence of serious mold problems in randomly chosen homes. Miller et al. (9) measured several indoor air biologic contaminants in 51 Canadian homes, of which 70 percent were selected because of prior complaints of indoor air problems. In six homes, the concentration of airborne colony-forming units exceeded 1,000/m<sup>3</sup>. Potentially hazardous species, *Aspergillus fumigatus* and *Stachybotrys atra*, were found in three homes.

Thus, although the associations between respiratory symptoms and home dampness or molds are probably causal, doubt remains because of the subjective nature of questionnaire reporting and because there is insufficient knowledge to accurately identify and measure the pathogenic molds.

Upper respiratory symptoms and eye irritation were also associated with home dampness/mold in the present study, suggesting that an airborne irritant or allergen is involved in the pathogenesis. House dust mites may be partly responsible for these adverse health effects. Although it is assumed that they do not occur on a broad scale in Canadian homes because of the cold, dry winters, there may exist humid microenvironments, such as damp basements, suitable for both molds and house dust mites

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(5). Inconsistent with an immediate hypersensitivity mechanism was the observation that the symptom and exposure association persisted despite stratification for the presence of diagnosed allergies to molds and dust. It would have been expected that those with reported allergies would have more symptoms on exposure to dampness, molds, or dust mites than those who reported no allergies. This was not the case. In addition, asthma which is partly an allergic disease in children was not as strongly related to home dampness or molds as were other health indicators. Allergic products of molds or dusts are recognized to cause immediate hypersensitivity symptoms, but it did not seem to be driving the overall relation in our population study.

The nonspecific symptoms we and others have detected (fever and chills, headaches, myalgias, nausea, vomiting, and diarrhea), if not simply due to a reporting bias, may be a clue to the pathogenesis. Similar symptoms have been described in "humidifier fever" and "mycotoxicosis," both of which may be caused by exposure to mold products (3, 22).

These speculations based on our results and those of others require further etiologic studies of the adverse health effects associated with home dampness and molds. Considering the relatively high prevalence of home dampness or molds, approximately 38 percent, it is an important public health issue for the Canadian population. Further work is required to determine both the likely pathogenic agents and how best to measure them in the general population.

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Neas, L.M., Dockery, D.W., Ware, J.H., Spengler, J.D., Speizer, F.E., and Ferris, B.G., "Association of Indoor Nitrogen Dioxide with Respiratory Symptoms and Pulmonary Function in Children," American Journal of Epidemiology 134(2): 204-219, 1991.

The authors examined the possible effect of indoor exposure to nitrogen dioxide on the cumulative incidence of respiratory symptoms and pulmonary function level in a cohort of 1,567 white children (aged 7-11 years) in six U.S. cities from 1983 through 1988. The authors reported that the study results suggest "an association between measured levels of indoor nitrogen dioxide and the cumulative incidence of a combined indicator of respiratory symptoms." The authors claim that respiratory symptoms were linearly associated with indoor nitrogen dioxide exposure. The authors report an odds ratio of 1.40 "for an increase in nitrogen dioxide equivalent to that for a gas stove." The authors also report that "neither excluding parental illness from the model nor including an indicator for maternal smoking during pregnancy altered the adjusted odds ratio."

## Association of Indoor Nitrogen Dioxide with Respiratory Symptoms and Pulmonary Function in Children

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The effect of indoor nitrogen dioxide on the cumulative incidence of respiratory symptoms and pulmonary function level was studied in a cohort of 1,567 white children aged 7–11 years examined in six US cities from 1983 through 1988. Week-long measurements of nitrogen dioxide were obtained at three indoor locations over 2 consecutive weeks in both the winter and the summer months. The household annual average nitrogen dioxide concentration was modeled as a continuous variable and as four ordered categories. Multiple logistic regression analysis of symptom reports from a questionnaire administered after indoor monitoring showed that a 15-ppb increase in the household annual nitrogen dioxide mean was associated with an increased cumulative incidence of lower respiratory symptoms (odds ratio (OR) = 1.4, 95% confidence interval (95% CI) 1.1–1.7). The response variable indicated the report of one or more of the following symptoms: attacks of shortness of breath with wheeze, chronic wheeze, chronic cough, chronic phlegm, or bronchitis. Girls showed a stronger association (OR = 1.7, 95% CI 1.3–2.2) than did boys (OR = 1.2, 95% CI 0.9–1.5). An analysis of pulmonary function measurements showed no consistent effect of nitrogen dioxide. These results are consistent with earlier reports based on categorical indicators of household nitrogen dioxide sources and provide a more specific association with nitrogen dioxide as measured in children's homes. *Am J Epidemiol* 1991;134:204–19.

air pollutants; child; household air quality; lung; nitrogen dioxide; respiratory function tests; respiratory tract diseases

Nitrogen dioxide is a by-product of high-temperature combustion in air. While most outdoor locations have an annual mean below the National Ambient Air Quality

Standard of 100  $\mu\text{g}/\text{m}^3$  (53 ppb) (1), the concentration of nitrogen dioxide may exceed this level in homes with unvented gas- or kerosene-fueled appliances (2). Previously

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Abbreviations: 95 percent CI, 95 percent confidence interval; FEV<sub>25–75</sub>, forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FEV<sub>0.75</sub>, forced expiratory volume in three-fourths of a second; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity, in natural logarithm; OR, odds ratio; PM<sub>2.5</sub>, particulates with a mean aerodynamic diameter less than 2.5  $\mu\text{m}$ .

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published results from the Harvard Six Cities Study (3, 4) have described the associations between respiratory symptoms and pulmonary function in two cohorts of pre-adolescent children with indicators of indoor pollution sources determined from questionnaires: parental smoking, gas stoves, and kerosene heaters. While evidence of increased respiratory symptoms and lower lung function has been reported for passive smoke exposure, the association with nitrogen dioxide sources has been less consistent. Only reported respiratory illness before the age of 2 years was positively associated with the presence of nitrogen dioxide sources in two cohorts of children in the Harvard Six Cities Study. Some measures of pulmonary function were also depressed for children with unvented gas or kerosene appliances. The misclassification of exposure potentially could be diluting any effect of nitrogen dioxide sources in these studies (5). In this paper, we present results from a study of a subset of the second cohort of children enrolled in the Harvard Six Cities Study, in which each child's residential exposure to nitrogen dioxide was directly measured by indoor monitoring.

## MATERIALS AND METHODS

### Study population

The study population was drawn from a cohort of 6,273 children from six different communities: Watertown, Massachusetts; Kingston and Harriman, Tennessee; the Carondelet area of St. Louis, Missouri; Steubenville, Ohio; Portage, Wisconsin, and surrounding communities; and a random sample of schools in Topeka, Kansas. A parent-completed respiratory symptom questionnaire and a pulmonary function examination were initially administered in a staggered scheme across cities between September 1983 and June 1986. The following year in each city, a second questionnaire and pulmonary function examination were administered to all of these children who were still living in these communities. Between 1 year and 18 months later in the fall, the

parents received a third health questionnaire. All children in specific grades of public and private elementary schools within the geographically defined study areas were enrolled so as to obtain a sample of about 1,000 children in each city: the third and fourth grades in St. Louis and Topeka, second through fourth grade in Steubenville, and second through fifth grade in Watertown, Kingston, and Portage.

In each city, a stratified one-third random sample of the first questionnaire respondents was solicited to participate in a comprehensive program of indoor air quality measurements. These children also kept a diary of respiratory symptoms (results not presented here). The initial stratified sampling strategy was to obtain 70 percent smoking households and 70 percent households with a major nitrogen dioxide source (gas cooking stove or kerosene heater) as reported on the first respiratory symptom questionnaire. The achieved proportions, 58 percent smoking households and 48 percent households with a major nitrogen dioxide source, were lower than planned because of geographic differences in gas stove utilization and smoking. The sampling strategy minimized the association between nitrogen dioxide and passive smoking exposures by ensuring essentially equal proportions of current smoking homes in each nitrogen dioxide exposure stratum.

### Indoor air quality measurements

Indoor air measurements were made in each participating household in two consecutive 1-week sampling periods in winter (mid-November through March) and in summer (mid-May through September) (6). The present analysis will report associations between respiratory health and indoor nitrogen dioxide with indoor respirable particle treated as a covariate. An integrated nitrogen dioxide sample was collected each sampling week using Palmes' passive diffusion tubes (7, 8) in the kitchen, activity room, and child's bedroom. In the first three cities (Watertown, Kingston, and St. Louis), two

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separate 1-week samples were collected, while a single 2-week measurement for each season was collected in Steubenville, Portage, and Topeka. Preassembled monitoring kits were placed in a sample of homes each week and returned to the central laboratory for analysis. The monitoring kits included randomly assigned replicates (5 percent) and field blanks (5 percent). A few samples (<0.5 percent) were voided for errors in sampling or analysis. In addition, two samples with measurements less than field blanks were assumed to have not been properly exposed. The passive sampling device functioned continuously throughout the sampling period. Homes without at least one valid measurement for both nitrogen dioxide and respirable particulates ( $n = 26$ ) were excluded, leaving 1,844 children in the subsample. For children with at least one measurement, a value for any one missing season was imputed for either the winter ( $n = 42$ ) or the summer ( $n = 204$ ) (9) (see Appendix). An annual nitrogen dioxide average was then calculated as the geometric mean of the two seasonal estimates for each location, and a household annual nitrogen dioxide average was calculated as the arithmetic mean of the annual nitrogen dioxide averages for the three locations. Respirable particulates less than  $2.5 \mu\text{m}$  in diameter ( $\text{PM}_{2.5}$ ) were measured by a Harvard aerosol impactor (10), which ran continuously in the activity room except for 8 hours each weekday when the child was normally in school.

#### Racial, age, and completeness restrictions

The analysis was restricted to white children between the ages of 7 and 11 at the first examination with complete information on a series of covariates: parental education and respiratory illnesses, family size and composition, number of rooms, and maternal smoking during pregnancy. The racial restriction excluded 149 children (8.1 percent), age excluded a further 19 children (1.1 percent), and the completeness of data excluded a final 109 children (6.5 percent),

for a final sample size of 1,567 children (figure 1).

The composition of the eligible cohort varied slightly with each questionnaire. Since the indoor measurements were obtained during the final year, the analysis was restricted to those earlier questionnaires for which there were not subsequently 1) a change in residence, 2) a change in type of cooking stove, or 3) a change in the family smoking status (smoking vs. nonsmoking). The number of completed questionnaires for this sample over the course of the study was 1,115 for the first questionnaire, 1,221 for the second, and 1,286 for the third. The response rate for the third questionnaire was lower in homes with a nitrogen dioxide source (77 percent), primarily because of a poor overall response rate for a mail distribution of the third questionnaire in Watertown (53 percent). In the other cities, the questionnaires were handled through the schools, and the response rate for the third questionnaire in these five cities was accept-

#### New Cohort of the Harvard Six Cities Study

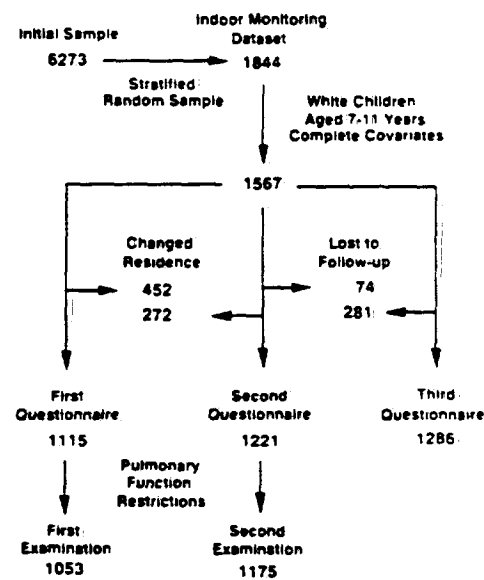


FIGURE 1. Schematic representation of the selection process and sample attrition, indoor monitoring dataset, Harvard Six Cities Study, 1983-1988. Changed residence implies either movement to a new residence or a major change in indoor pollutant sources.

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able in both homes with a nitrogen dioxide source (84 percent) and homes without a nitrogen dioxide source (90 percent).

#### Cumulative incidence of respiratory symptoms

Each questionnaire followed a standard format (11) and solicited responses to a series of questions on respiratory symptom prevalence during the year preceding the questionnaire. The third questionnaire was administered in the fall following the completion of the indoor air quality measurements and provides symptom information for the year during which the measurements were taken. A single binary variable was created that indicated the occurrence during the prior year of one or more of the following five lower respiratory symptoms: shortness of breath with wheezing, persistent wheeze, chronic cough, chronic phlegm, and bronchitis. Asthmatic status was based solely on a parental report of a physician's diagnosis and not on the presence of asthmatic symptoms. Hay fever and earache were reported separately. The chest illness and other illness variables reflect a restriction of the child's normal activities for 3 or more days. The other illness question excluded chest illness, but may have included upper respiratory illnesses.

#### Pulmonary function measurements

Measurements of pulmonary function have been discussed previously as an indicator of the effects of air pollutants (12). The pulmonary function measurements were conducted by trained spirometry field teams in the child's school using a recording survey spirometer (Warren E. Collins, Inc., Braintree, Massachusetts). After the child's weight and height in stocking feet were measured, each child performed at least five but not more than eight forced expiratory maneuvers while sitting with free mobility and without a noseclip. Unacceptable maneuvers were noted by the field team. Five pulmonary function parameters were considered: forced vital capacity (FVC), forced

expiratory volume at 1 second ( $FEV_{1.0}$ ), the ratio between  $FEV_{1.0}$  and FVC, forced expiratory volume at  $\frac{3}{4}$  second ( $FEV_{0.75}$ ), and forced expiratory flow between 25 percent and 75 percent of FVC ( $FEF_{25-75\%}$ ). The FVC and  $FEV_{1.0}$  measurements were calculated as the mean of the three best efforts that were within 150 ml of the largest measurement (13), and they were corrected to body temperature and pressure saturated (14).  $FEF_{25-75\%}$  was determined from the blow with the largest sum of FVC and  $FEV_{1.0}$ . A more detailed explanation of the measurement procedure has been provided previously (15).

#### Logistic regression model for respiratory symptoms

The logistic regression model estimated the effect of the measured level of nitrogen dioxide (annual household average in ppb) while controlling for the effects of city, sex, age at first examination, parental history of bronchitis or emphysema, parental history of asthma, parental college education, single parent family status, and the measured level of respirable particulates in the home (annual average in  $\mu\text{g}/\text{m}^3$ ). The child's age (7–11 years for the initial questionnaire) was dichotomized into either less than 10 years or 10 or more years of age (27 percent). Parental educational level was positive if the higher education parent living in the child's home had ever attended college (52 percent). Parental chronic obstructive pulmonary disease was positive if a history of bronchitis or emphysema was reported for either of the child's biologic parents (30 percent), while parental asthma was similarly positive for a reported history of asthma (12 percent). The analyses were conducted using SAS PROC LIFEREG with a logistic error distribution (16).

#### Basic pulmonary function regression model

The analysis of pulmonary function relied on a regression model developed by previous analyses of the Harvard Six Cities Study

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children's data (15). Each pulmonary function examination was analyzed separately. The natural logarithm ( $\ln$ ) of pulmonary function was modeled with a separate intercept for each of the six cities and included sex, parental education, parental history of asthma,  $\ln$  age,  $\ln$  height,  $\ln$  weight, and the interaction between sex and  $\ln$  height. The analyses were conducted using SAS PROC REG (16). In addition to the previous restrictions, the pulmonary function analysis was restricted to children who had complete anthropomorphic and pulmonary function measurements and whose height was 115–155 cm and whose weight was 45–135 lb (20.4–61.2 kg) for the first examination. For the second examination, these measurements were 120–160 cm and 50–150 lb (22.7–68.0 kg), respectively. These restrictions excluded 42 children from the first examination (3.8 percent) and 43 children from the second examination (3.3 percent). Regression analysis prior to the inclusion of the indoor pollution measures identified 10 children whose observed values differed from the predicted values by more than 4 standard errors. These children were excluded from further analyses. After the removal of these outliers, the measured levels

of nitrogen dioxide (annual household average in ppb) and respirable particulates (annual average in  $\mu\text{g}/\text{m}^3$ ) were added to the regression model. The final pulmonary function dataset included 1,053 children for the first examination and 1,175 children for the second examination (figure 1).

## RESULTS

### Univariate statistics

Table 1 provides descriptive statistics on exposures to indoor air pollutants for the restricted sample of 1,567 children by the presence of a major nitrogen dioxide source in the home for all six cities and by city. Overall, 48 percent of the children lived in homes with a major source of nitrogen dioxide; 83 percent of these children were exposed to a gas cooking stove and 21 percent to a kerosene heater. Homes with a major nitrogen dioxide source had higher proportions of current smokers (62 percent vs. 55 percent), boys (57 percent vs. 49 percent), and single parent families (16 percent vs. 14 percent), but lower proportions of parental chronic obstructive pulmonary disease (28 percent vs. 31 percent), parental asthma (11 percent vs. 13 percent), and one parent with

TABLE 1. Description of exposures by city and presence of a household nitrogen dioxide source (gas cooking stove or kerosene heater): Harvard Six Cities Study, 1983–1988

	Household nitrogen dioxide source	Total cohort (n)	% of children with a nitrogen dioxide source	Gas stoves (n)	Kerosene heaters (n)	Household nitrogen dioxide mean (ppb)			Current smoking household (n)	Annual respirable particulate mean ( $\mu\text{g}/\text{m}^3$ )
						Annual	Winter	Summer		
Six cities	No	816				8.6	8.9	9.2	446	31.8
	Yes	751	48	623	156	23.5	28.7	20.9	468	37.8
Watertown, MA	No	63				12.5	10.2	15.9	42	29.8
	Yes	162	72	162	1	27.9	31.5	25.5	118	35.6
Kingston, TN	No	173				6.1	7.3	5.9	73	42.2
	Yes	91	34	3	90	11.0	23.1	5.9	54	48.4
St. Louis, MO	No	69				16.0	15.4	17.7	38	37.3
	Yes	208	75	205	13	31.3	35.5	29.0	139	43.5
Steubenville, OH	No	148				11.4	11.7	12.3	100	33.6
	Yes	93	39	69	29	24.2	31.0	21.3	58	39.4
Portage, WI	No	194				5.7	5.9	6.1	95	24.6
	Yes	110	36	106	10	17.2	20.1	15.5	52	25.2
Topeka, KS	No	169				7.4	8.4	7.5	98	26.4
	Yes	87	34	78	13	16.7	21.4	14.2	47	31.3

a college education (46 percent vs. 57 percent). The annual mean concentration of respirable particles was also higher by  $6 \mu\text{g}/\text{m}^3$  in the homes with a nitrogen dioxide source.

The household annual average indoor nitrogen dioxide exposure concentration (figure 2) was 14.9 ppb higher for the 751 children living in homes with a major nitrogen dioxide source (mean  $\pm$  standard error =  $23.5 \pm 0.4$  ppb) than for the 816 children in the nonsource homes ( $8.6 \pm 0.2$  ppb). This excess was present in both winter ( $+19.8$  ppb) and in summer ( $+11.7$  ppb). In the homes with a major nitrogen dioxide source, the household average was 7.8 ppb higher in the winter, while in the homes without a major nitrogen dioxide source, the winter measurements were 0.4 ppb lower. Treitman et al. (17) suggested that these seasonal differences reflect decreased winter ventilation and a consequent decrease in the contribution of nitrogen dioxide from external sources. In homes with a major nitrogen

dioxide source, the annual average of the two seasonal nitrogen dioxide measurements (figure 3) was higher in the kitchen ( $28.8 \pm 0.6$  ppb) than in the activity room ( $21.6 \pm 0.4$  ppb) or the child's bedroom ( $19.8 \pm 0.4$  ppb). The room-specific indoor nitrogen dioxide measurements were highly correlated with Pearson correlation coefficients greater than 0.90, while the household annual averages for indoor nitrogen dioxide and  $\text{PM}_{2.5}$  were unrelated. Nitrogen dioxide enters the health effects models as a continuous variable, and the results are presented in this paper as the effect of a 15-ppb increase in the household annual average of the indoor nitrogen dioxide measurements, which is comparable to the crude difference between homes with and without a major nitrogen dioxide source (14.9 ppb).

The household annual indoor nitrogen dioxide averages were modeled using 1,159 children who had complete information on selected household characteristics from the second questionnaire. The final predictors included city, the number of rooms, and indicator variables for gas cooking stove.

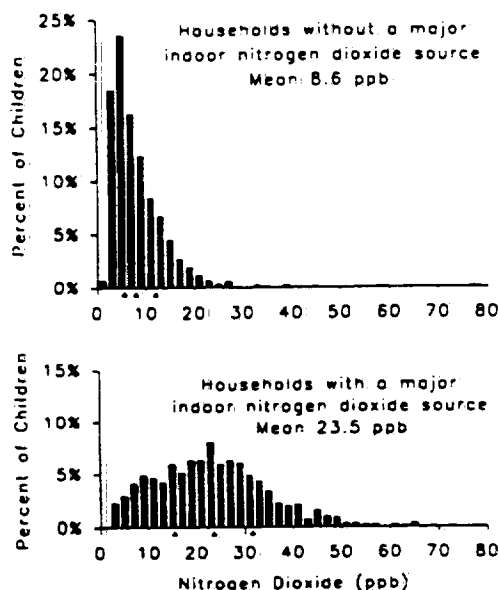


FIGURE 2. Household average nitrogen dioxide measurements by the report of a major indoor nitrogen dioxide source (gas stove or kerosene heater) on the third questionnaire: Harvard Six Cities Study, 1983-1988. Quartiles of the nitrogen dioxide distribution are indicated by triangles below the axis.

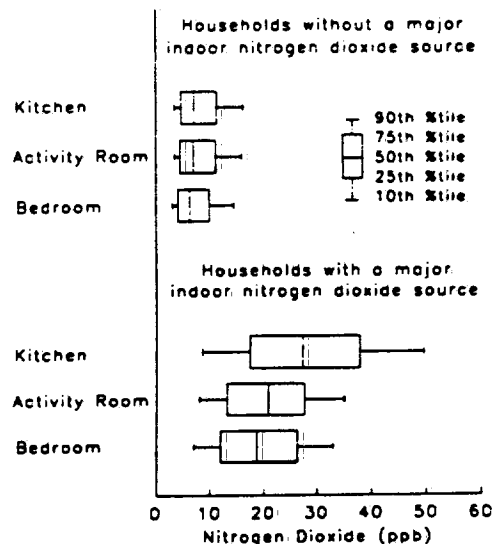


FIGURE 3. Distribution of percentiles for the annual average indoor nitrogen dioxide concentration by room location of the sampler and the report of a major indoor nitrogen dioxide source (gas stove or kerosene heater) on the third questionnaire: Harvard Six Cities Study, 1983-1988.

type of gas fuel, pilot lights, kitchen fan, kerosene space heater, wood stove, and current smoking status. The other variables considered were the use of the cooking stove for heating and the type of fuel used by the main heating system. The final model explained 68 percent of the variation in the measured annual average indoor nitrogen dioxide level and predicted a 17.3-ppb increase in nitrogen dioxide for households using a gas cooking stove with pilot lights. Kerosene space heaters that are typically used only during winter contributed much less (+2.7 ppb) to the annual average nitrogen dioxide level, as did smoking in the home (+1.7 ppb). The nitrogen dioxide measurements were weakly associated with parental education and single parent family status, but not with the child's age or sex or with parental illness.

On the third questionnaire, physician-diagnosed asthma was reported for 6 percent of the children, but asthmatic symptoms were reported twice as frequently: 12 percent for persistent wheeze and 13 percent for shortness of breath with wheeze. The cumulative incidences of chronic cough (8 percent), chronic phlegm (9 percent), and bronchitis (9 percent) were similar. The cumulative incidence of restriction of normal activity for 3 or more days for chest illness (11 percent) was comparable to that for other nonchest illnesses (12 percent). The most common symptoms reported were earache (34 percent) and hay fever (24 percent). The proportion of missing data for each symptom never exceeded 6 percent and was generally 4 percent or less.

#### **Effect of nitrogen dioxide on the annual cumulative incidence of respiratory symptoms**

The presence of a major nitrogen dioxide source showed a similar crude association with each of the five lower respiratory symptoms on the third questionnaire (table 2): shortness of breath with wheeze (odds ratio (OR) = 1.24), persistent wheeze (OR = 1.25), chronic cough (OR = 1.29), chronic phlegm (OR = 1.35), and bronchitis (OR =

1.24). Positive associations were not found for asthma, hay fever, earache, or restrictions of activity due to either chest illness or other illness. The composite measure of lower respiratory symptoms had a crude odds ratio of 1.38 (95 percent confidence interval (95% CI) 1.05–1.53).

The logistic regression model described earlier was applied to estimate the effect of a 15-ppb difference in indoor nitrogen dioxide on each of the symptoms. The adjusted odds ratios were similar to the crude relative risks associated with the presence of a major nitrogen dioxide source. The composite indicator of lower respiratory symptoms had a statistically significant association with indoor nitrogen dioxide. When expressed as the effect of a 15-ppb increase in the household annual average of the nitrogen dioxide measurements in the child's home, the adjusted odds ratio was 1.40 (95 percent CI 1.14–1.72).

Over the 3 years of questionnaires, the cumulative incidence rates of lower respiratory symptoms increased among children in homes with a major nitrogen dioxide source: 22 percent in the first, 24 percent in the second, and 29 percent in the third. Rates were stable for the children living in non-source homes: 21 percent, 21 percent, and 23 percent. The crude relative odds of lower respiratory symptoms increased steadily over the three questionnaires (1.05, 1.17, and 1.38), as did the adjusted odds ratios (0.90, 1.21, and 1.40).

When the third questionnaire was analyzed separately by sex, an increased effect of nitrogen dioxide was seen among the girls (OR = 1.68, 95 percent CI 1.30–2.19) compared with boys (OR = 1.16, 95 percent CI 0.89–1.51). Similarly, the nitrogen dioxide effect appears to be stronger among children with current domestic exposure to passive cigarette smoke (OR = 1.48, 95 percent CI 1.19–1.84) compared with those in non-smoking homes (OR = 1.22, 95 percent CI 0.89–1.66).

When the analysis was repeated separately for each city (table 3), the estimates of the effect of a 15-ppb increase in nitrogen dioxide on lower respiratory symptoms were

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**TABLE 2.** Annual cumulative incidences and crude odds ratios (ORs) associated with a major indoor nitrogen dioxide source (gas stove or kerosene heater) and the adjusted odds ratios and 95% confidence intervals (95% CIs) associated with a 15-ppb increase in the annual average indoor nitrogen dioxide exposure by symptom: Harvard Six Cities Study, 1983-1988

	Effect of nitrogen dioxide source category			Effect of a 15 ppb difference in nitrogen dioxide, adjusted*	
	Cumulative incidence (%)		Crude OR	OR	95% CI
	No source	Source			
Shortness of breath	11.5	13.9	1.24	1.23	0.93-1.61
Chronic wheeze	11.3	13.8	1.25	1.16	0.89-1.52
Chronic cough	7.6	9.5	1.29	1.18	0.87-1.60
Chronic phlegm	8.2	10.7	1.35	1.25	0.94-1.66
Bronchitis	7.8	9.4	1.24	1.05	0.75-1.47
Lower respiratory symptoms	22.8	29.0	1.38	1.40	1.14-1.72
Asthma	7.1	5.4	0.75	0.91	0.60-1.36
Hay fever	24.0	24.7	1.04	0.98	0.79-1.22
Earache	34.5	33.0	0.94	1.09	0.90-1.32
Chest illness	10.5	11.0	1.06	1.10	0.83-1.46
Other illness	12.3	12.5	1.02	1.06	0.81-1.40

\* Odds ratios adjusted for city, sex, age, parental history of bronchitis or emphysema, parental history of asthma, parental college education, single parent family status, and the measured levels of respirable particulates in the home.

**TABLE 3.** Annual cumulative incidences of lower respiratory symptoms and crude odds ratios (ORs) associated with a major indoor nitrogen dioxide source (gas stove or kerosene heater) and the adjusted odds ratios and 95% confidence intervals (95% CIs) associated with a 15-ppb increase in the annual average indoor nitrogen dioxide exposure by city: Harvard Six Cities Study, 1983-1988

	Effect of nitrogen dioxide source category			Effect of a 15 ppb difference in nitrogen dioxide, adjusted*	
	Cumulative incidence (%)		Crude OR	OR	95% CI
	No source	Source			
Watertown, MA	14.3	15.5	1.10	1.27	0.59-2.72
Kingston, TN	22.4	42.9	2.60	1.32	0.63-2.77
St. Louis, MO	27.8	23.2	0.79	1.27	0.88-1.85
Steubenville, OH	29.0	39.0	1.57	1.44	0.97-2.13
Portage, WI	17.7	26.9	1.71	1.86	1.13-3.04
Topeka, KS	24.7	34.3	1.59	1.26	0.72-2.20

\* Odds ratios adjusted for city, sex, age, parental history of bronchitis or emphysema, parental history of asthma, parental college education, single parent family status, and the measured levels of respirable particulates in the home.

nearly equal in spite of a considerable variation in the city-specific prevalence of major nitrogen dioxide sources as shown in table 1.

A consistent pattern also was found when the analysis was repeated separately for each source category (table 4). For this table, the classification of households was based on any mention of a major indoor nitrogen dioxide source on either the second or the third questionnaire, that is, before or after the indoor monitoring. The estimated effect of a 15-ppb increase in the annual average

indoor nitrogen dioxide exposure was slightly lower among the 495 children from gas stove homes compared with the 181 children from homes with kerosene heaters. The estimated nitrogen dioxide effect was slightly lower among the 630 children from homes without any report of a major nitrogen dioxide source on either questionnaire. The nitrogen dioxide effect estimate for non-source homes was dominated by a single home's high nitrogen dioxide level (58.3 ppb). Deleting this observation reduced the maximum value of the average annual in-

door nitrogen dioxide concentration to 35.6 ppb and reduced the estimated odds ratio for nonsource homes to  $OR = 1.01$  (95 percent CI 0.44–2.32).

To check the modeling of nitrogen dioxide as a continuous variable, nitrogen dioxide measurements were collapsed into four ordered exposure categories of approximately equal size (table 5). The mean nitrogen dioxide levels varied from 3.7 ppb in the lower exposure category to 31 ppb in the upper exposure category, while the presence of a major household nitrogen dioxide source varied from 9 percent to 93 percent. The relative odds for lower respiratory symptoms increased monotonically with the mean nitrogen dioxide level.

#### Effect of nitrogen dioxide on pulmonary function measurements

The pulmonary function measures were conducted in conjunction with the first two questionnaires and preceded the indoor pol-

lutant measurements. No pulmonary function measurements were made in conjunction with the third questionnaire following the indoor monitoring. For an additional 15 ppb of nitrogen dioxide, the only association which reached statistical significance was an increase in  $FEV_{10}/FVC$  among boys ( $p < 0.04$ ). There was no indication that nitrogen dioxide exposure was associated consistently with a reduction in any of the pulmonary function measures (table 6).

## DISCUSSION

### Previous studies

Unvented gas household appliances have been reported in US and European studies to be associated with increased respiratory symptoms in children. In a study of 5,758 English children aged 6–11 years, Melia et al. (18) reported that gas cooking stoves were associated with the increased prevalence of six respiratory symptoms among boys

TABLE 4. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) associated with a 15-ppb increase in the annual average indoor nitrogen dioxide exposure by major indoor nitrogen dioxide source category as reported on a questionnaire either before or after indoor air sampling: Harvard Six Cities Study, 1983–1988

Nitrogen dioxide source category	No. of children	Nitrogen dioxide level (ppb)		Adjusted*	
		Range	Mean	OR	95% CI
Gas stove	495	2.1–78.2	24.5	1.37	1.02–1.84
Kerosene heater	181	2.6–69.3	13.2	1.45	0.82–2.56
No reported major indoor source	630	1.7–58.3	7.5	1.23	0.62–2.47

\* Odds ratios adjusted for city, sex, age, parental history of bronchitis or emphysema, parental history of asthma, parental college education, single parent family status, and the measured levels of respirable particulates in the home.

TABLE 5. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) associated with ordered indoor nitrogen dioxide exposure categories on the annual cumulative incidence of lower respiratory symptoms: Harvard Six Cities Study, 1983–1988

Nitrogen dioxide level (ppb)		Nitrogen dioxide source (%)	No. of children	Cumulative incidence (%)	Adjusted*	
Range	Mean				OR	95% CI
0–4.9	3.7	9	263	22.8	1.00	
5–9.9	7.3	20	360	24.2	1.06	0.71–1.58
10–19.9	14.4	50	317	27.1	1.36	0.89–2.08
20–78.2	31.0	93	346	27.8	1.65	1.03–2.63

\* Odds ratios adjusted for city, sex, age, parental history of bronchitis or emphysema, parental history of asthma, parental college education, single parent family status, and the measured levels of respirable particulates in the home.

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TABLE 6. Percentage of change in selected pulmonary function measurements and 95% confidence intervals (95% CIs) associated with a 15-ppb increase in the annual average indoor nitrogen dioxide exposure by examination and sex: Harvard Six Cities Study, 1983-1988

	First examination		Second examination	
	% of change*	95% CI	% of change	95% CI
<b>Males</b>				
FVC†	-0.7	-2.0 to +0.6	-0.4	-1.6 to +0.8
FEV <sub>1.0</sub> †	+0.1	-1.3 to +1.5	-0.1	-1.5 to +1.3
FEV <sub>1.0</sub> /FVC	+0.8	+0.0 to +1.6	+0.3	-0.5 to +1.1
FEV <sub>0.75</sub> †	+0.1	-1.4 to +1.5	-0.1	-1.6 to +1.3
FEF <sub>25-75%</sub> †	+1.8	-1.1 to +4.6	+0.7	-2.2 to +3.5
FEF <sub>25-75%</sub> /FVC	+2.5	-0.3 to +5.2	+1.1	-1.7 to +3.8
<b>Females</b>				
FVC	+0.7	-0.8 to +2.2	-0.6	-2.0 to +0.7
FEV <sub>1.0</sub>	+0.9	-0.6 to +2.4	-0.2	-1.6 to +1.1
FEV <sub>1.0</sub> /FVC	+0.2	-0.6 to +1.0	+0.4	-0.3 to +1.1
FEV <sub>0.75</sub>	+0.7	-0.9 to +2.3	-0.3	-1.7 to +1.1
FEF <sub>25-75%</sub>	+0.3	-3.0 to +3.4	+0.1	-2.7 to +2.8
FEF <sub>25-75%</sub> /FVC	-0.5	-3.7 to +2.7	+0.7	-2.1 to +3.4

\* Percentage of change adjusted for city, parental history of asthma, parental college education, in age, in weight, and in height.  
 † FVC, forced vital capacity; FEV<sub>1.0</sub>, forced expiratory volume in 1 second; FEV<sub>0.75</sub>, forced expiratory volume in three-fourths of a second; FEF<sub>25-75%</sub>, forced expiratory flow between 25 and 75% of FVC, in natural logarithm.

(OR = 1.27, 95 percent CI 1.08-1.50) and girls (OR = 1.39, 95 percent CI 1.16-1.65), after controlling for age and social class. After controlling for 28 geographic areas, the association remained significant for girls ( $p < 0.05$ ), but not for boys ( $p \sim 0.30$ ). Subsequent studies by Keller et al. (19) of 441 Columbus, Ohio, families and by Schenker et al. (20) of 4,071 Pennsylvania children failed to detect any significant associations between gas stoves and the incidence or prevalence of respiratory symptoms. In fact, Keller and coworkers found a protective effect for gas stoves that may have been an artifact of controlling for the child's prior illness history. If chronic exposure to nitrogen dioxide is a risk factor for early childhood illnesses, controlling for the child's illness history will substantially reduce the estimated effect of current nitrogen dioxide exposures. Dodge (21) found a very large excess prevalence (OR = 2.2,  $p < 0.05$ ) of cough associated with gas stoves in a study of 676 children in three Arizona communities.

Gas stoves have shown an association with respiratory symptoms among an earlier cohort of children participating in the Harvard Six Cities Study. In a preliminary report on

8,120 children, Speizer et al. (22, 23) found that gas cooking stoves were significantly associated with respiratory illness prior to age 2 (OR = 1.12, 95 percent CI 1.00-1.26). In a follow-up analysis of a larger cohort of 10,106 of these children, Ware et al. (3) reported that a similar association was found between gas stoves and respiratory illness prior to age 2 (OR = 1.13, 95 percent CI 0.99-1.28), which was slightly reduced by an adjustment for parental education (OR = 1.11, 95 percent CI 0.97-1.27). No significant associations were found for any reports of respiratory symptoms in the previous year, including chronic cough, persistent wheeze, and bronchitis. For a second sample of 6,273 children in the six cities from which the participants in the present study were selected, Dockery et al. (4) reported that physician-diagnosed respiratory illness prior to age 2 was significantly associated with gas cooking stoves with pilot lights (OR = 1.22, 95 percent CI 1.02-1.47) and marginally associated with kerosene heaters (OR = 1.11, 95 percent CI 0.89-1.37). No associations were found with individual respiratory symptoms in the previous year as reported on the first questionnaire. Neither gas stoves nor kerosene heat-

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ers were associated with differences in pulmonary function measurements. Ekwo et al. (24) also have found an increased prevalence (OR = 2.4, 95 percent CI 1.4–4.1) of hospitalization for respiratory illness before age 2 among 1,138 Iowa City children.

Measured levels of indoor nitrogen dioxide also were reported to have an association with respiratory symptoms in children. Florey et al. (25) reported that the prevalence of a combined indicator of respiratory symptoms was not associated with kitchen nitrogen dioxide levels among 428 children in gas cooking homes, but was associated with bedroom nitrogen dioxide levels among a subsample of 80 children ( $p < 0.10$ ). In a 1982 follow-up study of children living in 183 gas cooking homes, Melia et al. (26) reported that living room nitrogen dioxide measurements were significantly associated with the prevalence of respiratory conditions at the 90 percent confidence level, but bedroom nitrogen dioxide measurements showed no significant association. In a 1987 study of 121 children under the age of 13 years, Berwick et al. (27) reported an association between living room nitrogen dioxide measurements over 16 ppb and increased reporting of eight lower respiratory symptoms among children under 7 years, but not among children 7 years and older after controlling for socioeconomic status and history of respiratory illness. As with the study by Keller et al., Berwick's control for prior respiratory illnesses may have weakened any association with nitrogen dioxide exposure.

In a 1990 study of 775 Dutch children aged 6–12 years, Dijkstra et al. (28) found no association between mean indoor nitrogen dioxide concentrations and a combined indicator of one or more of three lower respiratory symptoms: chronic cough, any mention of wheeze, and attacks of shortness of breath with wheeze. The nitrogen dioxide measurements were collected over 1 week in January, compared with the 2 weeks of measurements in both the winter and summer seasons used for the present study. The 1-week winter samples of Dijkstra et al. provide a less reliable estimate of each child's

exposure to nitrogen dioxide over the entire year. The range of exposures was somewhat smaller with only 79 (10 percent) children (eight of whom had one or more symptoms) who lived in homes with a 1-week average winter measurement more than 32 ppb of nitrogen dioxide, compared with 195 (15 percent) of the 1,286 children in the present study with a 2-week average winter concentration above 32 ppb. Nevertheless, there is no clear explanation at this time for the lack of association in this study.

Pulmonary function measurements have not shown a consistent association with either gas stoves or with direct measurements of nitrogen dioxide exposure. Hasselblad et al. (29) reported a decline in pulmonary function among 3,000 girls aged 9 through 13 years ( $-1.1$  percent  $FEV_{0-5}$ ), but a slight increase among 3,552 boys aged 9 through 13 years ( $+0.3$  percent  $FEV_{0-5}$ ). In a longitudinal analysis of 7,834 children in the Harvard Six Cities Study cohort, Berkey et al. (30) reported slight declines in both FVC ( $-0.55$  percent, 95 percent CI  $-1.16$  percent to  $+0.05$  percent) and  $FEV_{1.0}$  ( $-0.41$  percent, 95 percent CI  $-1.03$  percent to  $+0.02$  percent) for both sexes combined. Slightly greater than predicted levels of pulmonary function were found in the study of Vedal et al. (31) of 1,631 children living in gas stove homes ( $+0.1$  percent  $FEF_{25-75\%}$ ). In an English study of 485 children, Florey et al. (25) found no association between kitchen nitrogen dioxide measurements and pulmonary flow measurements after adjustment for age, height, weight, and sex, although girls in gas cooking homes had significantly higher values of peak expiratory flow and  $FEF_{25-75\%}$ .

### Present study

The present study is in substantial agreement with these previous studies in finding an association between measured levels of indoor nitrogen dioxide and the cumulative incidence of a combined indicator of respiratory symptoms. In this study, lower respi-

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ratory symptoms were linearly associated with indoor nitrogen dioxide with an odds ratio of 1.40 for an increase in nitrogen dioxide equivalent to that for a gas stove. This is similar in magnitude to the previously reported effect of passive smoke exposure. For example, Ware et al. (3) report a relative odds of 1.23 for the association between maternal smoking and an index of lower respiratory illness in an earlier cohort in these cities. The association is stronger among girls and among children living in smoking homes, but the effect is still present among boys and among children living in nonsmoking homes. Melia et al. (26) found a stronger association among girls between gas stove exposure and respiratory symptoms. The lack of a significant adverse effect on pulmonary function is in agreement with the results of Berkey et al. (30) and Vedal et al. (31). These findings appear to indicate that either the increased prevalence of respiratory symptoms due to nitrogen dioxide exposure does not lead to any impairment of pulmonary function or the impairment of pulmonary function is a delayed or rare result of nitrogen dioxide exposure, but they are in agreement with the lack of a consistent finding of reduced pulmonary function among children with viral bronchiolitis (32), a condition which is similar to the toxic bronchiolitis that may be produced by acute nitrogen dioxide poisoning.

The nitrogen dioxide effect is remarkably consistent when the analysis is repeated separately for each city and each nitrogen dioxide source category (tables 3 and 4). Such consistency implies that other factors, such as climate and social class that may be associated with city or source category, do not strongly confound the nitrogen dioxide effect estimate. In particular, this consistency is striking, given the wide variation in the actual nitrogen dioxide exposure levels across city and source categories. This suggests that nitrogen dioxide is a common linkage in the observed health effects, even though a more toxic by-product of indoor nitrogen dioxide may be the primary irritant. Pitts et al. (33) have suggested that nitrogen dioxide reacts with interior surfaces

to produce nitrous acid. In either case, indoor nitrogen dioxide is specifically implicated, whether directly affecting symptom reporting or indirectly through the production of nitrous acid.

Alternatively, selective inclusion or exclusion of participants is a potential source of bias due to the loss of children over the 3 years of the study. Complete measurements for indoor pollutants were not obtained for all of the households initially selected for inclusion in the indoor air quality monitoring study, but these sampling losses were not associated with differences in household source characteristics. Children were also lost to follow-up because of failure to obtain all three questionnaires. In large part, this attrition was because of school busing in St. Louis and the poor response to a mail distribution of the third questionnaire in Watertown. Neither of these is likely to have been strongly associated with nitrogen dioxide exposure. The overall symptom prevalence rate increased over the course of the study, which may be due to either parents with asymptomatic children losing interest in participating in the study or parents who did not accurately complete the initial symptom questionnaires withdrawing from the sample in subsequent years. In any case, the two cities with the highest retention rates, Steubenville (88 percent) and Portage (99 percent), had the highest city-specific estimates for the association of nitrogen dioxide with lower respiratory symptoms.

A second alternative explanation for these findings is that other variables associated with both nitrogen dioxide exposure and respiratory symptom reporting, i.e., confounders, may be producing a spurious association. The strongest confounder in this study was socioeconomic status, and controlling for this and other potential confounders in the model actually increases the association from a crude odds ratio of 1.38 to an adjusted odds ratio of 1.40. Family size, the presence of younger siblings, and the number of persons per room were found to have no significant effect when considered for inclusion in the model. Neither excluding parental illness from the model nor in-

cluding an indicator for maternal smoking during pregnancy altered the adjusted odds ratio.

Home wetness was also considered as a potential confounder. Goldstein et al. (34) reported that unvented gas appliances raise humidity and cause surface condensation in the home that may act independently to increase respiratory symptoms. In a cohort of 4,625 children from which the children in the current study were selected, Brunekreef et al. (35) reported that home dampness indicators were significantly associated with increased reporting of respiratory symptoms. In the indoor air-monitoring sample, home dampness indicators were associated with the combined indicator of lower respiratory symptoms, but only weakly associated with nitrogen dioxide. Controlling for the effects of home dampness did not modify the association of lower respiratory symptoms with the indoor nitrogen dioxide concentrations.

The misclassification of children with regard to either exposure or symptoms also may have introduced a bias. As the symptom measurements become more remote in time from the indoor monitoring, the observed effect of nitrogen dioxide appears to diminish. This may be due to either a systematic bias or may represent a real temporal variability of the results. The increased rate of symptom reporting over the three questionnaires by parents with a major nitrogen dioxide source could be explained by overreporting as these parents became aware of the hypothesized association of respiratory illness and gas stoves. However, such a bias would not explain the dose-response association found with level of nitrogen dioxide nor the consistent associations found when the children were considered separately by source class. An alternative explanation for this trend is that there was increasing nondifferential misclassification of exposure, i.e., the indoor nitrogen dioxide concentration, as the questionnaires become more remote in time from the indoor measurements during the final year of the study.

For any exposure assessment scheme, the highest observed levels are produced by a

process that involves both the average exposure level in the home and the chance occurrence of unusually high exposure events. As the number of samples and the duration of the sampling period are increased, chance deviations in the nitrogen dioxide level make less of a contribution to the estimated annual average nitrogen dioxide exposure level. In this study, the collection of samples over a 2-week period in both the winter and summer provides a better estimate of each child's long-term average nitrogen dioxide exposure than samples collected over a single winter week. By reducing the contribution of chance events to the exposure assessment, repeated measurements over an extended period reduce the nondifferential misclassification of children with regard to exposure and, thus, the bias toward the null which such misclassification generally introduces into the effect estimate.

Questionnaire responses are also subject to recall biases and nondifferential misclassification. Recall bias is also suggested by the higher rates of the child's respiratory symptoms by parents with asthma or chronic obstructive pulmonary disease. However, these parental illnesses were not correlated with the nitrogen dioxide measurements and, thus, cannot bias the associations with nitrogen dioxide. Even with the use of a standardized questionnaire of respiratory symptoms, parents apply different interpretations of the symptom questions in reporting their children's symptoms. For example, the parent's choice between reporting chronic cough, chronic phlegm, and/or bronchitis may be related to factors other than their child's actual symptom history. Thus, it is appropriate to consider not only specific symptoms but also composite measures that combine data from correlated symptoms with related physiologic bases. In this study, the lower respiratory symptom complex combines data from several correlated symptoms that are characteristic of lower rather than upper respiratory tract illnesses, reducing misclassification between symptoms.

This study provides evidence that nitrogen dioxide concentrations in the home are as-

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sociated with increased parental reporting of lower respiratory symptoms in children. However, no permanent changes in lung airways associated with nitrogen dioxide were detected with standard pulmonary function examinations. These findings are consistent with reports from previous studies that have used indicators of indoor nitrogen dioxide sources other than direct measurements of indoor concentrations. The monotonic increase in the reporting of lower respiratory symptoms with the ordered nitrogen dioxide exposure categories (table 5) implies that nitrogen dioxide has adverse health effects at levels below the current ambient outdoor standard of 53-ppb annual mean. Since the specific toxic agent may be a product of subsequent reaction of nitrogen dioxide on indoor surfaces to produce acid gases, future investigations of the indoor chemistry of nitrogen dioxide may suggest alternative mitigation techniques. However, this study suggests that a direct reduction of indoor nitrogen dioxide exposures would have health benefits: i.e., the relative odds of lower respiratory symptoms would drop by 29 percent for each 15-ppb decrease in the annual mean indoor nitrogen dioxide concentration. Such exposure reductions could come through the control of indoor nitrogen dioxide sources, through the removal of nitrogen dioxide from outdoor air infiltrating into the home, and through the reduction of ambient nitrogen dioxide concentrations.

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## APPENDIX

### Imputation of indoor air quality values for a single missing season

For the kitchen measurements of nitrogen dioxide, 1,358 (87 percent) of the restricted cohort of 1,567 children had at least one valid measurement in each season, and 768 (57 percent) of these had two valid measurements in one or both seasons. An additional 196 children had valid measurements of kitchen nitrogen dioxide for one season but had no valid measurements in the other season: 34 children in the winter and 162 children in the summer. The other sampling locations had similar patterns of missing values. For respirable particulates, 1,318 of the children had at least one valid measurement in each season, and 1,277 of these had two valid measurements in one or both seasons. An additional 222 children had valid measurements of respirable particulates for one season but had no valid measurements in the other season: 72 children in the winter and 150 children in the summer. The increase in missing values during the summer was generally due to difficulties in scheduling the sampling with respect to family vacations.

The replicate measurement of each indoor pollutant in both seasons for the majority of the children's homes permits the imputation of values for homes with no valid measurements for a single season. The algorithm for computing these imputed values comprises the following steps.

- 1) For the sample of all individuals ( $i = 1$  to  $n_j$ ,  $n_i < n_j$ ) with two observations in a single season ( $j$ ), calculate an estimate of the between-week variance for each season ( $j$  and  $j'$ ):

$$S_{unijj'}^2 = \sum 1/2 (X_{i1j} - X_{i2j})^2 / (n_j - 1)$$

- 2) For each season ( $j$  and  $j'$ ) and each individual ( $i = 1$  to  $n_j$ ,  $n_j > n_j'$ ) with at least one

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observation in that season, calculate a seasonal mean and a seasonal between-week variance:

$$\text{If two observations: } \bar{X}_{ij} = (X_{i1j} + X_{i2j})/2$$

$$\phi_{ij}^2 = (X_{i1j} - X_{i2j})^2/4$$

$$\text{If one observation: } \bar{X}_{ij} = X_{i1j}$$

$$\phi_{ij}^2 = s_{imij}^2$$

3) For the entire sample of all individuals ( $i = 1$  to  $n^*$ ,  $n_i > n^* > n_j$ ) with at least one observation in both seasons, calculate a grand mean for each season ( $j$  and  $j'$ ):

$$\bar{X}_j = \sum \bar{X}_{ij}/n^*$$

4) For the entire sample of all individuals ( $i = 1$  to  $n^*$ ,  $n_i > n^* > n_j$ ) with at least one observation in both seasons, calculate the slope and intercept of a prediction equation that will impute the seasonal mean for a season with no valid observations from the seasonal mean of a season with one or more valid observations ( $j$  and  $j'$ ):

$$\text{Slope: } \hat{\gamma}_{1j} = \frac{\sum (\bar{X}_{i1} - \bar{X}_1)(\bar{X}_{i2} - \bar{X}_2)}{\sum [(\bar{X}_{i1} - \bar{X}_1)^2 - \phi_{i1}^2]}$$

$$\text{Intercept: } \hat{\gamma}_{0j} = \bar{X}_j - \hat{\gamma}_{1j}\bar{X}_j$$

5) For the entire sample of all individuals ( $i = 1$  to  $n^*$ ,  $n_i > n^* > n_j$ ) with at least one observation in both seasons, calculate the season error variance for each season ( $j$  and  $j'$ ):

$$\hat{\sigma}_{j'}^2 = \frac{\sum [(\bar{X}_{i1} - \bar{X}_1) - \hat{\gamma}_{1j}(\bar{X}_{i1} - \bar{X}_1)]^2 - \hat{\gamma}_{1j}^2 \phi_{i1}^2}{n^* - 2}$$

6) For each individual ( $i = 1$  to  $n_j^0$ ) with no valid observations in a single season ( $j$ ), but at least one observation in the other season ( $j'$ ), impute a mean and a between-week variance for the missing season ( $j$ ):

$$\bar{X}_{i1} = (\bar{X}_{i2} - \hat{\gamma}_{0j})/\hat{\gamma}_{1j}$$

$$\phi_{i1}^2 = (\phi_{i2}^2 + \hat{\sigma}_{j'}^2)/\hat{\gamma}_{1j}^2$$

7) For each individual ( $i = 1$  to  $n$ ,  $n > n_j$ ) with at least one observation in either season, calculate the annual mean:

$$\bar{X}_i = (\bar{X}_{i1} + \bar{X}_{i2})/2$$

8) For each individual ( $i = 1$  to  $n^*$ ,  $n > n^* > n_j$ ) with at least one observation in both seasons, calculate an annual variance:

$$\psi_i^2 = (\phi_{i1}^2 + \phi_{i2}^2)/4$$

For each individual ( $i = 1$  to  $n_j^0$ ) with no valid observations in a single season ( $j$ ), but at least one observation in the other season ( $j'$ ), impute an annual variance:

$$\psi_i^2 = \left[ \phi_{i2}^2 + \left( 1 + \frac{2}{\hat{\gamma}_{1j}^2} \phi_{i2}^2 \right) \right]/4$$

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Soderstrom, M., Hovelius, B., and Prellner, K., "Children with Recurrent Respiratory Tract Infections Tend to Belong to Families with Health Problems," Acta Paediatr Scand 80: 696-703, 1991.

Forty-one children aged 7-11 years who had recurrent respiratory tract infections (RTI) treated with antibiotics as preschoolers, and their families were compared with regard to medical and social factors to families with children (n=29) of comparable age who had had no such infections as preschoolers, or only isolated episodes. The authors conclude that "the results of the present study support the idea that children with recurrent bacterial RTIs as preschoolers tend to belong to families with health problems."

## Children with Recurrent Respiratory Tract Infections Tend to Belong to Families with Health Problems

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**ABSTRACT.** Söderström, M., Hovellius, B. and Prellner, K. (Department of Community Health Sciences, Dalby, and Department of Oto-Rhino-Laryngology, University of Lund, Sweden). Children with recurrent respiratory tract infections tend to belong to families with health problems. *Acta Paediatr Scand* 80: 696, 1991.

Children (7-11 years of age) who had recurrent respiratory tract infections (RTI) treated with antibiotics as preschoolers ( $n=41$ ), and their families were compared with regard to medical and social factors to families with children of comparable age who had had no such infections as preschoolers, or only isolated episodes (controls:  $n=29$ ). All the children studied had attended day-care centres as preschoolers. The two groups of children did not differ with regard to socio-economic conditions or age at admission to day-care centres. There was a difference in the two groups with regard to signs noted at physical examination ( $p<0.05$ ), eardrum changes being observed in 34% of the children with recurrent episodes of RTI as preschoolers and in none of the controls ( $p<0.001$ ). Questionnaires answered by parents indicated diseases, particularly cardiovascular diseases, to be significantly more frequent in the families of the children with recurrent RTIs as preschoolers than in those of the controls ( $p<0.01$ ). Parents of the controls were more often satisfied with their own health ( $p<0.05$ ) and reported fewer symptoms of minor illness ( $p<0.05$ ), as compared with parents of the children with recurrent RTIs as preschoolers. Thus, the results of the present study support the idea that children with recurrent bacterial RTIs as preschoolers tend to belong to families with health problems. *Key words:* respiratory tract infection, family health, day-care centre.

Some preschool children seem to be exceptionally prone to recurrent respiratory tract infections (RTI) while others remain relatively free from such infections. A relationship has been suggested to exist between the frequency of RTI and a number of factors, such as sex and age of the child, family size (1), socio-economic status (2), parental smoking (3, 4), acute or persistent family stress (5) and form of day-care attended by the child (6, 7). A close relationship has been found to exist between "child physician utilization" and "maternal physician utilization" (8).

The aim of the study has been to assess some medical and social factors in families with children who as preschoolers attended day-care centres and had recurrent episodes of antibiotic-treated RTI, and compare these with a control group of families with children who had no such RTI or only isolated episodes. The assessment was done by means of a questionnaire answered by the parents, clinical examination of the children, and scrutiny of their medical records.

### SUBJECTS AND METHODS

Of 395 school-age children belonging to the 1975-79 birth cohorts, who had attended day-care centres as preschoolers (1980-82), and who had been prospectively followed owing to their participation in a study of pneumococcal immunization (9), 70 children were enrolled in the present study which started in 1986. The children included in the immunization study were recruited from 66 day-care centres in the municipalities of Lund attended by approximately 4000 children. Children with chronic or progressive diseases or known immunological disor-

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ders had been excluded, as had children with cleft palate. On the basis of their infection history during the day-care period, two age-matched groups were selected: one group, defined as RTI-afflicted as preschoolers (i.e.,  $\geq 4$  episodes of RTI treated with antibiotics during the years 1980–82), and a control group, where the children included were defined as non-RTI-afflicted as preschoolers (i.e.,  $\leq 2$  episodes of RTI treated with antibiotics during the 1980–82 period, and  $\leq 2$  episodes prior to their enrolment in the immunization study in 1980).

Of the 135 children thus selected, 19 had moved from the Lund area in the interim, leaving 116 children and their families to be invited to participate in the two-year follow-up study. Participation was declined in 46 cases (22 children with a high number of antibiotic-treated RTIs and 24 with no antibiotic-treated RTI or only isolated episodes), the most common reasons given for non-participation being lack of time and aversion for blood, throat and nasopharyngeal sampling. Of the remaining 70 children 41 were included in the group of RTI-afflicted children (25 boys, 16 girls; mean age = 9.1 years; median age = 9 years) and 29 in the control group (19 boys, 10 girls; mean age = 9.0 years; median age = 9 years). They were invited to a physical examination, accompanied by one of their parents who answered a questionnaire. Nineteen (46%) of the RTI-afflicted children and 19 (68%) of the control group had been vaccinated during the immunization study with the 14-polyvalent pneumococcal vaccine. The difference in proportion between the groups was nonsignificant.

Medical histories from birth to the start of the present study were collected from one or more of the following sources after permission from the parents: the paediatric, ear-nose-throat and infectious diseases clinics, local community health centres and the emergency reception centre.

The physical examination included a routine check of the skin, lymph-nodes in the neck, of the respiratory system, and the heart. The ear-nose-throat examination included otomicroscopy and screening audiography (20 dB). Blood pressure was measured with a cuff of appropriate size after 10 min of rest. Body mass index was determined. Children with cardiac murmur were re-examined by a paediatric cardiologist.

**Questionnaire.** Parents gave written answers to the questionnaire prior to the examination of their child at the community health centre. The investigator (M. S.) checked that all questions were answered. The questionnaire was designed to elicit details concerning family size, age of parents and sibling(s), length of time the children had been solely breast-fed (i.e., no supplementary bottle), age at admission to day-care centres, living conditions, family smoking habits, socio-economic status, the educational level of both parents and current school situation of the child. The classification of the socio-economic status in the two groups was based on the occupations of the parents (10).

The parents were asked to list any occurrence of infections, allergy, kidney disease, gastrointestinal disease, cardiovascular disease (hypertension, myocardial infarction, angina pectoris, stroke), diabetes mellitus, rheumatoid arthritis, cancer or other diseases in the family (parents, grandparents and siblings). They were also asked about what they perceived as chronic disease, among themselves, the enrolled child, and its siblings.

The parents' attitude to their own current situation was elicited with a question concerning their satisfaction with their own health, current family situation, family economy, social life, and quality of leisure time activities. A five-point Likert scale was employed: very satisfied, reasonable satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, very dissatisfied. The occurrence of minor symptoms of illness (headache, abdominal pain, dizziness, and sleeping disorders) experienced by the child or the parent at least once every fortnight, were noted (yes or no answers). Any sick leave taken by either parent during the past twelve months was also reported.

**Statistical methods.** Either Fisher's exact test or the Mann-Whitney's rank sum test (one or two-tailed, depending on the question) was used to compare data from the two groups.

## RESULTS

**Respiratory tract infections in the children.** The mean number of antibiotic-treated RTIs per child from birth to the end of the immunization study (1982) was 12.2 (median = 13; range = 4–23; quartiles  $Q_1=8$ ,  $Q_3=15$ ) in the RTI-afflicted children and 1.4 (median = 1; range = 0–4;  $Q_1=Q_3=0$ ) in the control group. The mean number of antibiotic-treated RTIs from birth to the start of the present study (1986) for the two groups of children were 16.7 (median = 16; range = 6–31;

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Q1–Q3=11–21) in the RTI-afflicted children and 2.6 (median = 2; range = 0–7; Q1–Q3=0.5–4) in the control group. The majority of antibiotic-treated RTIs had been diagnosed as acute otitis media, acute tonsillitis, purulent nasopharyngitis, bronchitis or bronchopneumonia. One child among the RTI-afflicted had been treated for a *Haemophilus influenzae* epiglottitis.

*Clinical findings among the children.* As shown in Table 1, various signs were observed more frequently in the RTI-afflicted children than in the controls. One child from the control group had a ventricular septum defect. Cardiac murmur in 16 children was diagnosed as being of physiological origin. One of the RTI-afflicted children had unilateral total deafness following an episode of parotitis, and another had a neurogenic hearing defect. No hearing impairment was found among the remaining children. There was no difference in systolic/diastolic blood pressure between the group of RTI-afflicted children as preschoolers and controls (109/60 (SD = 10/11) and 109/59 (SD = 9/14), respectively). Body mass index was identical: 16.8 (kg/m<sup>2</sup>) (SD = 2.2) for both groups.

*Familial and social factors.* The questionnaire was generally answered by the mother, in 35 (85%) of the cases in the RTI-afflicted group and in 26 (89%) of the cases in the control group. The two groups differed little with regard to family characteristics (Table 2). The mean age of parents in both groups was equal. Most of the children were living in single-family dwellings (private houses). Two families with RTI-afflicted children had changed their living conditions since 1982 because of the illness of their children and had moved to the countryside. Ten children belonging to the RTI-afflicted group, compared to none in the control group ( $p < 0.01$ ), had shifted from day-care centres to family day-care or home care during the preschool years, in two cases the reason being the child's recurrent RTIs. For the remaining children the reason was a change in the family situation, e.g., a baby was born into the family. One child among the RTI-afflicted and two of the controls required special assistance at school in such basics as reading, writing and mathematics.

*Family health.* Significantly more diseases, particularly cardiovascular diseases,

Table 1. Signs noted at routine physical examination of school-age children with a history of recurrent respiratory tract infection (RTI-afflicted as preschoolers) as compared with controls

Signs	RTI-afflicted <i>n</i> = 41 (%)	Controls <i>n</i> = 29 (%)	Difference*
Enlarged tonsils	9 (22)	2 (7)	NS
Sclerotic plaque, scarred eardrum(s) or tympanostomy tubes	14 (34)	0	$p < 0.001$
Palpated lymphoglandulae in the neck	14 (34)	9 (31)	NS
Pulmonary ronchi, auscultatory abnormalities	7 (17)	3 (10)	NS
Cardiac murmur	11 (27)	6 (20)	NS
Eczema, atopic skin	8 (20)	3 (10)	NS
Any combination of the above	30 (73)	13 (45)	$p < 0.05$

\* Fisher's exact test (two-tailed).

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were reported in the families of RTI-afflicted children than in those of controls (Table 3). Hypertension was reported in 19 grandparents of the RTI-afflicted and in 5 grandparents of the control children. Angina pectoris/myocardial infarction was reported in 30 grandparents of the RTI-afflicted children and in 10 of the control children, respectively. Three parents of RTI-afflicted children, but none of the parents of controls, reported themselves to be suffering from a chronic disease (malignant melanoma, leucopenia with recurrent infectious diseases, and spondylosis). Siblings of five RTI-afflicted children were reported to have a chronic disease, as compared with two siblings of controls (NS; Fisher's exact test, one-tailed).

Parents of the RTI-afflicted children were less satisfied with their own health than were parents of controls ( $p = 0.03$ ; Mann-Whitney rank sum test, one-tailed). Nineteen (66%) parents of the controls described themselves as very satisfied with their health, as compared with 17 (41%) of the parents of RTI-afflicted children. There were no differences between the groups with regard to the remaining com-

Table 2. Social and demographic factors relating to children (7–11 years of age) with a history of recurrent respiratory tract infections as preschoolers (RTI-afflicted) as compared with controls

	RTI-afflicted ( $n=41$ ) $n$ (%)	Controls ( $n=29$ ) $n$ (%)	Difference
<i>Family characteristics</i>			
Average family size (per.)	4.1 (SD=0.6)	4.2 (SD=0.8)	NS
No. of first-born children in group	22 (54)	10 (35)	NS
No. of single children in group	7 (17)	2 (7)	NS
Divorced/non-divorced	4/37	4/25	NS
<i>Socio-economic characteristics</i>			
<i>Father</i>			
Manual worker	4 (10)	8 (28)	NS
Non-manual employee or self-employed	37 (90)	21 (72)	NS
University educated	32 (78)	13 (45)	$p < 0.01$
<i>Mother</i>			
Manual worker	10 (24)	5 (17)	NS
Non-manual employee	31 (76)	24 (83)	NS
University educated	23 (56)	17 (59)	NS
<i>Living conditions</i>			
Single-family house	35 (85)	26 (89)	NS
Building constructed after 1974	21 (51)	10 (35)	NS
<i>Other factors</i>			
Father currently a smoker	11 (27)	7 (24)	NS
Mother currently a smoker	4 (10)	9 (31)	$p < 0.05$
Smoking at home > 5 cigs/day	8 (20)	7 (24)	NS
Breast-fed only (months)	3.6 (SD=2.6)	3.7 (SD=2.9)	NS
Average age (months) at admission to day-care centre	21.5 (SD=13.4)	23.8 (SD=16.5)	NS

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mon matters (work, current family situation, social life, and quality of leisure time activities).

The number of parents who stayed at home sick at least once during the previous twelve months did not differ significantly between the two groups (28% and 20% of the RTI-afflicted and control groups, respectively). Both parents had stayed at home sick in 5 of 37 (14%) families of RTI-afflicted children, as compared with 1 of 25 (4%) families of controls (NS: Fisher's exact test, one-tailed).

Reported symptoms of minor illness (Table 4) were more frequent among parents of RTI-afflicted children than among those of controls.

Table 3. Number of relatives (parents, siblings and grandparents) with diseases, as reported by parents to 41 RTI-afflicted children as preschoolers and 27 children in a control group

Type of disease	Number of relatives in		p-value <sup>a</sup>
	RTI-afflicted group (n=293) n (%)	Control group n=195 n (%)	
Infectious diseases	20 (7)	5 (3)	0.36
Allergic diseases	40 (14)	17 (9)	0.31
Rheumatoid arthritis and other immunological diseases	11 (4)	4 (2)	0.46
Cardiovascular diseases	51 (17)	17 (9)	0.009
Diabetes mellitus	7 (2)	1 (1)	0.45
Cancer	7 (2)	2 (1)	0.47
Any combination of the above	117 (40)	39 (20)	0.002

<sup>a</sup> Two adopted children excluded.

<sup>b</sup> Mann-Whitney rank sum test, two-tailed.

Table 4. Symptoms of minor illness occurring relatively often (at least once a fortnight) in parents (P) and children (C), as reported by parents of 41 RTI-afflicted children as preschoolers and 29 controls. (Figures given are number of instances, with percentages in brackets.)

Symptoms	RTI-afflicted		Controls	
	P n=40 <sup>a</sup> n (%)	C n=40 <sup>a</sup> n (%)	P n=29 n (%)	C n=29 n (%)
Headache	12 (30)	5 (13)	5 (17)	2 (7)
Abdominal pain	7 (18)	5 (13)	1 (3)	1 (3)
Insomnia	3 (8)	0	1 (4)	3 (10)
Dizziness	2 (5)	0	0	0
Any combination of the above	19 (48) <sup>b</sup>	7 (18)	7 (24) <sup>b</sup>	4 (14)

<sup>a</sup> One parent declined to answer these questions.

<sup>b</sup> p<0.05 (Fisher's exact test, one-tailed).

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## DISCUSSION

The present results suggest that children who have suffered from recurrent bacterial RTIs as preschoolers belong to families in which morbidity is high and health problems generally prevalent. This might be a reflection of environmental factors and/or genetic predisposition, involving increased susceptibility both to RTI and to other diseases. The tendency to report symptoms of minor illness and take sick leave more often in the families with a RTI-afflicted child than in those of the controls lends additional support to the conclusion that children who had recurrent bacterial RTIs as preschoolers belong to families with health problems.

It may be argued that the method used did not select children who had recurrent RTI only, but also included children using the medical services frequently for other reasons. However, 80% of the children's physician attended visits 1980-82 were made to one of two experienced ear-nose-throat doctors, which supports the assumption that the majority of the episodes treated with antibiotics were of bacterial etiology. Furthermore, the ear drum changes found in 34% of the children defined as RTI-afflicted as preschoolers may be regarded as sequelae of otitis media, which suggests that these children had had bacterial infections to a higher extent than had the controls.

As all the children studied attended day-care centres as preschoolers, they had had similar opportunities to be exposed to contagious agents. Other studies have shown that younger children attending day-care centres contract more infections than do older ones (6, 7, 11), which is also true of children not attending day-care centres (1). As the average age at admission to day-care centres did not differ between the two groups, this factor hardly explains the difference in the frequency of RTI. In a recent study, Harsten et al. (12) found that the child's age at the initial episode of acute otitis media, and not his or her attendance at day-care centres seemed to be the major indicator of susceptibility to recurrent otitis media.

Despite the selected character of our study population, the social background was largely the same for the RTI-afflicted children and the controls, and typical of families with children attending day-care centres in Sweden (13).

The smoking habits of parents, particularly those of mothers, have been related to both upper and lower RTI and to impaired pulmonary function among their growing children (3, 14). In the present study, however, fewer of the mothers of RTI-afflicted children were still smokers than were mothers of controls. The habit of smoking has been reported to have declined among educated people in Sweden in recent years (15). Thus, the mothers of children defined as RTI-afflicted as preschoolers in our study may have changed their smoking habits owing to their child's susceptibility to RTI, while the need to stop smoking might not have appeared as urgent to the mothers of controls. Accordingly, the effect of passive smoking on the frequency of RTI during the day-care period of the children could not be evaluated.

The impact of pneumococcal vaccination is another factor possibly affecting susceptibility to RTI (9). The difference between the groups concerning number of children immunized and of those given placebo was non-significant in the present study, but the percentage of immunized children was somewhat higher in the control group. The immunization study showed a reduction in the overall frequency of upper RTI in children older than two years at vaccination (9).

In this study, we found diseases to be more frequent in the families of children who had been RTI-afflicted as preschoolers than in those of controls, which may indicate that genetic factors play a role. Familial aggregation, both of cardiovascular

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diseases, cancer and otitis media has been reported (16, 17, 18, 19). Our findings seem to support the assumption that some families are more vulnerable than others to disease. According to Huygen's (20) experience from his family practice during 30 years, families do not only differ in their readiness to call for professional medical help, but also in their readiness to fall prey to all kinds of diseases.

All parents, except those of the adopted children, answered the questions concerning diseases in the extended family. It might be argued, however, that the reliability of the information about family health, usually provided by the mothers, might have differed between the groups of parents. A family with a child suffering frequently from bacterial RTIs may have more occasions to consider or discuss diseases, not only that of the child but also those of other members of the family; thus such parents might tend to report family disease history more exhaustively than parents of healthy controls. Mothers of low socio-economic status tend to apply a selective censorship when informing about family health (21). As the social background was equal among mothers in both groups we found no reason to believe that the accuracy of information given concerning family health would differ.

Another important aspect is the consequences of recurrent RTIs. Even if several of the RTI-afflicted children had suffered many episodes of acute otitis media affecting the eardrums, they manifested no hearing impairment for that reason and were doing well at school, findings supported by some studies indicating that recurrent otitis media do not result in lasting developmental impairment (22).

In conclusion, we found recurrent antibiotic-treated RTIs in the children studied to be more related to the prevalence of health problems in their respective families than to social or demographic factors. As some families are more vulnerable to diseases than others, it seems to be valuable for the physicians to be attentive to the health problems in the family of a child consulting for recurrent RTIs.

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2023510390

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Koenig, J.Q., Larson, T.V., Hanley, Q.S., Rebolledo, V., Dumler, K., Checkoway, H., Wang, S.Z., Lin, D.Y., and Pierson, W.E., "Human Health and Environmental Effects. Session 136. Woodsmoke Exposure and Human Health Impacts: Pulmonary Function Changes in Children Associated with Particulate Matter Air Pollution From Woodsmoke," Proc Annul Meet Exhib Air Waste Manage Assoc 15A(84): 2-8, 1991.

The authors of this study investigated respiratory function in 313 children (including 26 with asthma) exposed to particulate matter from woodsmoke emitted from woodburning stoves during two heating seasons. The authors stated that "this analysis clearly indicates that increases in air pollution are associated with declines in children's pulmonary function" and that "there is growing evidence that exposure to constituents of wood smoke affect pulmonary function in young children." The authors reported that the associated effects were "far greater" in asthmatic children than in nonasthmatic children. Removing children reportedly exposed to parental smoking did not change the analysis.

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**Pulmonary Function Changes in Children  
Associated with Particulate Matter Air  
Pollution from Wood Smoke**

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### Introduction

Air pollution composed of fine particulate matter may be a risk factor for decreased lung function and increased prevalence of respiratory disease symptoms, especially in young children under 12 years of age. For instance, a two year study of the relationship between pulmonary function changes in third and fourth grade children and air pollutant alerts in Steubenville, Ohio, found a decline in pulmonary function tests associated with increasing 24-hour concentrations of total suspended particulate matter (TSP)<sup>1</sup>. Peak values of TSP ranged from 27  $\mu\text{g}/\text{m}^3$  to 422  $\mu\text{g}/\text{m}^3$ . The pulmonary function declines were small but persisted for up to two weeks. Similar findings were reported from the Netherlands in a study of children aged 6-11 years before and during an air stagnation episode<sup>2</sup>. Data reported by Ware and associates<sup>3</sup> show increased respiratory symptoms in children aged 6 through 9 years exposed chronically to elevated levels of particulate matter (as well as sulfur dioxide).

The sources of particulate matter in the above studies were mainly industrial and automotive. Another growing source of particulate matter in residential neighborhoods is wood burning stoves and fire place inserts. Many communities, including Seattle, have geographical areas with high concentrations of fine particulate matter from wood burning during the winter heating season. There is wide-spread concern that this source of air pollution may cause or aggravate respiratory illness.

Studies in the US have explored the relationship between wood smoke and health. Monicky and co-workers<sup>4</sup> conducted a survey study of 31 preschool children who lived in homes using wood stoves and 31 children whose homes had no wood stoves. A significant increase in severity of respiratory symptoms was seen in the exposed children. Butterfield et al.<sup>5</sup> also found increased symptoms, especially wheezing, in children living in homes with wood stoves. The use of a wood-burning stove was found to be a risk factor for lower respiratory tract infection in American Indian children<sup>6</sup>.

The evidence is not completely consistent, however. Tuthill et al.<sup>7</sup> found no association between wood stove usage and symptoms of respiratory disease. A limitation of prior research is that none of the above studies provided either indoor or outdoor air monitoring data.

Larson et al.<sup>8</sup> measured particulate matter less than 10 micrometers ( $\text{PM}_{10}$ ) emitted by wood burning devices for three heating seasons at a residential site in north Seattle. Due to the topography of the city, some areas along creek drainages have quite high accumulations of  $\text{PM}_{10}$  on clear nights, whereas nearby areas on ridges have 2-3 times lower concentrations. A questionnaire study conducted in both these areas suggested that

young children aged 1-5 years living in the high wood smoke area had a pattern of more respiratory symptoms and disease than similar children living in the less polluted area<sup>9</sup>. In order to evaluate further possible respiratory effects on children, we conducted repeated spirometric measurements in young children differentially exposed to wood smoke during two heating seasons. Statistical analysis clearly indicated a strong association between light scattering coefficient, a surrogate of PM<sub>10</sub>, and declines in pulmonary function. This was true for all children, but the association was much stronger in children with asthma. We conclude that exposure to fine particulate matter from wood burning stoves in residential neighborhoods causes decreased pulmonary function in young children. A preliminary report of these data was presented last year<sup>10</sup>.

#### Methods

The study extended over two heating seasons, 1988-89 and 1989-90. The subjects during the first study year were 313 children, including 26 with asthma, from two participating elementary schools drawn from the target area. During the second study year, only 26 children with asthma were studied. Fourteen of these asthmatics had been studied in year one; the remaining 12 children had either graduated to seventh grade or moved from the schools. Consent forms describing the study were sent home with all third through sixth grade children. In the first year, all children who returned a signed consent were studied; in year two, all asthmatics whose parents consented were studied. Table 1 summarizes pertinent characteristics of the children.

Questionnaires were sent to nonparticipants to determine whether they differed as a group from participants. Nonparticipants mainly did not enter the study because they did not receive the form. There were no differences regarding parental smoking, presence of asthma, or household use of a wood heat between the two groups.

Spirometry was measured in each school during morning recess or the lunch hour on four occasions. From these records forced expiratory volume in one second (FEV<sub>1</sub>) and forced vital capacity (FVC) were calculated. Height was measured at each period, and the child was asked if he or she had been ill during the preceding week. Information on parental smoking, the presence of a wood stove in the home, allergy, or asthma were obtained on the consent form. Baseline lung function measurements prior to the heating season were conducted in September. The lung function measurements were gathered again in the first week of December, and third week of February, and the third week of May. During year two, additional measurements were made in December 1989 and in January 1990.

The spirometers used were three OHIO 822s and one Vitalograph. Even though the Vitalograph spirometer was



computerized, all tracings were hand calculated to be comparable with the manual spirometers. Each child was asked to perform three acceptable tracings. The best FEV<sub>1</sub> and FVC from each record was used. All values were converted to standard body temperature pressure saturated (BTPS) values.

Air monitoring data during the first study year were collected with integrating nephelometers at three sites, one each in the high and low wood smoke areas and one intermediate site. Also filter samples collected using Harvard-EPRI samplers with 2.5  $\mu$ m inlets. Light scattering coefficient (bsp) has been shown to be highly correlated with PM<sub>10</sub> at these residential locations ( $r^2 = .9$ ).<sup>8</sup> For the statistical analysis, the nephelometer record from the high wood smoke site for the day preceding each functional measurement period was used. A random effects model for repeated measures was selected for studying the relationship between bsp and FEV<sub>1</sub> or FVC. The model is based on the method described by Laird and Ware<sup>11</sup> and was carried out by the Restricted Maximum Likelihood Estimation (REML) program obtained from the Harvard School of Public Health. The logarithmic transformation was performed on the light scattering (bsp) data before model fitting in order to alleviate the skewness of the bsp distribution. Since each child acts as his/her own control in the growth curve models, no adjustments for individual characteristics (e.g. height, gender) are necessary.

#### Results

Air monitoring data from the high wood smoke area show that the average PM<sub>10</sub> from November, 1988 to March, 1989 in the first study year was 44  $\mu$ g/m<sup>3</sup>. During the second study year, there were frequent windy days and the average PM<sub>10</sub> was lower, 38  $\mu$ g/m<sup>3</sup>. The average light scattering values during the first and second heating seasons for the day preceding lung function measurements were 2.46 and 0.81  $\times 10^{-4}$  respectively.

Table 1 shows the grade distribution of the 343 children who participated in study. The table also shows the number of children with asthma, allergy, parental smoking, and household use of wood heat.

The estimates of the population slopes for bsp versus FEV<sub>1</sub> and FVC are shown in Table 2. Because of significant interactions between asthmatic status and the slopes, separate results are presented for asthmatic and nonasthmatic children. All slopes are significant with greater significance found for values from children with asthma. The relationship between FEV<sub>1</sub> and FVC and light scattering is significant at the 1% and 5% level respectively. The results for children with no parental smoking, not shown here, were similar to those of all children, indicating that parental smoking was not a confounding factor.

Table 1. Characteristics of the Children

	N	Allergy w/o Asthma	Asthma		Smoker in home	Wood heat in home
			1988- 89	1989- 90		
Third Grade	109	18	7	5	13	40
Fourth Grade	61	16	6	4	14	20
Fifth Grade	98	10	7	6	12	40
Sixth Grade	67	23	6	7	14	22
Total N	335	67	26	22	53	122

Table 2. Estimates of slopes for FEV<sub>1</sub> and FVC versus light scattering coefficient.

	Asthmatics		Nonasthmatics	
	FEV <sub>1</sub>	FVC	FEV <sub>1</sub>	FVC
Slope estimate (Liters)	-0.089	-0.097	-0.026	-0.032
Standard error	0.026	0.025	0.011	0.010
Slope/std error (Liters/(10 <sup>-4</sup> /M)	-3.401*	-3.96*	-2.35#	-3.19*

\* p = 0.01 level

# p = 0.05 level

### Discussion

This analysis clearly indicates that increases in air pollution are associated with declines in children's pulmonary function. In addition, these effects are far greater for asthmatic children than for nonasthmatic children. There is growing evidence that exposure to constituents of wood smoke affect pulmonary function in young children. The pollutants emitted into the air when wood is burned are products of incomplete combustion. In this regard, wood smoke resembles environmental tobacco smoke, for which numerous studies have shown deleterious effects on respiratory health of children<sup>12</sup>. Both pollutants contain nitrogen oxides, carbon monoxide, benzo(a)pyrene, aldehydes and various polycyclic aromatic hydrocarbons<sup>13</sup>. In the present study, the fine particulate matter portion of wood smoke pollution (b<sub>sp</sub>), which was found to be highly associated with depressions in pulmonary function over the heating season. However, it is possible, that fine particulate matter is not the only constituent of wood smoke which is a respiratory irritant.

There is one report of considerable acidity in wood smoke particles<sup>14</sup>. A recent study in the Seattle air shed measured hydrogen ion from filters placed in the high wood smoke area of our health effects study<sup>15</sup>. There is evidence that fine particles in the form of sulfuric acid cause decreases in pulmonary function in adolescent asthmatic subjects after a brief 45 minute exposure<sup>16</sup>. Therefore it is biologically plausible that aerosol acidity was responsible for the effect seen in this study.

In studies of associations between air pollutants and respiratory health, it is always possible that some confounding variables are biasing the outcome. Our analysis indicated that removing data from children exposed to parental smoking did not change the analysis.

Another important result of this study, is the increased risk from community pollution attendant to children with asthma. Table 3 shows that the associations between bsp and both FEV<sub>1</sub> and FVC changes are much stronger for children with asthma than for their nonasthmatic peers. Other studies of the effects of community air pollution on respiratory health in children also have suggested increased susceptibility among asthmatics. Dockery and co-workers<sup>17</sup> reported that chronic cough, bronchitis and chest illness were positively associated with fine PM, including fine sulfates, in a group of children studied in the Harvard Six City Study. Although the association between PM and symptoms in asthmatic children was not significantly different from the nonasthmatic children, the authors concluded there was a stronger association. With regard to pulmonary function, Stern and others<sup>18</sup> reported significantly lower FEV<sub>1</sub> and FVC values in children aged 7-12 when comparing two communities with different levels of air pollution. They also saw a significant relationship between air pollution and wheeze, and a significant relationship between use of a gas cooking stove and asthma.

Since the air monitoring period chosen in this study was the evening before the pulmonary function measurements for each child, our results most likely indicate an acute effect of the air pollutant rather than a chronic one.

We conclude that the airborne concentration of fine particulate matter measured by light scattering in a wood burning community is strongly associated with retardation in pulmonary function growth in children exposed during a winter heating season. Further more, the relationship is strongest for children with asthma.

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Holberg, C.J., Wright, A.L., Martinez, F.D., Ray, C.G., Taussig, L.M., Lebowitz, M.D., and Group Health Medical Associates, "Risk Factors for Respiratory Syncytial Virus-associated Lower Respiratory Illnesses in the First Year of Life," American Journal of Epidemiology 133(11): 1135-1151, 1991.

The authors performed a study of 1,179 healthy infants to examine the possible relationship between breastfeeding and other factors to the incidence of respiratory syncytial virus-associated lower respiratory tract illness (RSV-LRI) in the first year of life. For children between the ages of 1 and 3 months, the risk of having an RSV-LRI was associated with <1-month or no breast feeding, male sex, and increasing numbers of others sharing the child's bedroom. After multivariate analysis, only male sex and number of others sharing the bedroom remained as significant direct effects. Daycare attendance was reportedly a significant risk factor in the 7 to 9 month age group. The authors reported that "those with lower cord serum RSV antibody, who also have minimal breast feeding, were found to be especially at risk for RSV-LRIs in the first five months of life."

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## Risk Factors for Respiratory Syncytial Virus-associated Lower Respiratory Illnesses in the First Year of Life

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Lynn M. Taussig,<sup>1-3</sup> Michael D. Lebowitz,<sup>1,5</sup> and Group Health Medical Associates<sup>6</sup>

The relation of breast feeding and other factors to the incidence of respiratory syncytial virus-associated lower respiratory tract illness (RSV-LRI) in the first year of life is examined. The study population is 1,179 healthy infants enrolled at birth between May 1980 and January 1984 into the Tucson Children's Respiratory Study, Tucson, Arizona. Each subject's data were assessed at each month of age during the first year of life, during those months when respiratory syncytial virus was isolated. A number of significant relations were observed, particularly between 1 and 3 months of age. At this age, the risk of having a RSV-LRI increased in association with <1-month or no breast feeding, with being male, and with increasing numbers of others sharing the child's bedroom. In multivariate analysis, only sex and the number of others sharing the room remained as significant direct effects. However, a significant interaction demonstrated that breast feeding has a protective role in relation to RSV-LRIs for those infants of mothers with a lower education level. The risk of having a RSV-LRI increases with combinations of risk factors. Being in day care was a significant risk factor in the 7- to 9-month age range. The RSV-LRI rate also varies by birth month. A separate case-control study assessed relations of RSV-LRIs with cord serum RSV antibody. Those with lower cord serum RSV antibody, who also have minimal breast feeding, were found to be especially at risk for RSV-LRIs in the first 5 months of life. *Am J Epidemiol* 1991;133:1135-51.

breast feeding; bronchiolitis; respiratory syncytial viruses; respiratory tract infections; risk factors

Respiratory syncytial virus (RSV) is a major cause of serious life-threatening illness of the lower respiratory tract in infancy (1). It is responsible for yearly epidemics, of approximately 5-month duration, which are

closely associated with an increase in the numbers of infants and young children hospitalized with lower respiratory tract illnesses (LRI) (2).

While a variety of risk factors have been

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Abbreviations: CI, confidence interval; LRI, lower respiratory tract illness; OR, odds ratio; RR, relative risk (ratio); RSV, respiratory syncytial virus; RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness.

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shown to be related to RSV infection (3, 4), these factors have not always been examined concurrently or on a monthly basis. Risk factors studied include sex, ethnicity, number of siblings and crowding, socioeconomic status, birth weight, maternal smoking, seasonality and birth month, and other social and family factors.

A protective effect of breast feeding against hospitalization due to RSV infection has been demonstrated by some studies (5). However, this effect has not always been statistically significant when controlling simultaneously for a number of confounders (4). No significant differences were found, in a nonhospitalized population, in the rates or distributions of infection with RSV in relation to feeding practices (6); however, trends toward decreased morbidity in the breast-fed group were present, especially in the early months of life. These effects have also been shown to vary with infant age and the amount and exclusivity of breast feeding (7-10).

A number of studies have shown an inverse relation between severity of RSV infection and levels of antibody in sera collected near the time of onset of illness (3, 11). Additionally, higher antibody titers at birth are associated with an older age at the time of infection (3) and lower rates of RSV infection in the first 6 months of life (12). Some studies, such as that by Toms et al. (13), suggest that maternal antibodies may act indirectly by protecting the mother and, hence, reducing the risk of viral transmission to the infant in the first month of life; others would suggest a more direct role for maternal antibody (14). Also, human colostrum has been shown to contain neutralizing activity against RSV in vitro (5, 15). Conversely, results of trials of inactivated RSV vaccine in infants have led to the suggestion that antibodies against some components of RSV may be involved in the pathogenesis of severe bronchiolitis (12, 16). However, the relations of breast feeding or breast milk and cord serum antibody titer to RSV infections have not been examined concurrently in a community population of infants.

We have examined many of these factors

in the Tucson Children's Respiratory Study. The Children's Respiratory Study is a prospective study of respiratory illness in childhood, investigating the risk factors for and sequelae of acute LRIs in a large cohort of infants followed from birth (17, 18). The aim of the present investigation is to examine, prospectively, in this predominantly outpatient population of infants the possible interrelations of breast feeding, RSV antibody at birth, and other factors (sex, ethnicity, maternal education, the number of others sharing the child's room, maternal smoking, and day care) to the incidence of respiratory syncytial virus-associated lower respiratory tract illnesses (RSV-LRIs) in the first year of life.

Two approaches are used in our analyses: 1) In the total population, relations are assessed between RSV-LRIs and all risk factors considered, except cord serum RSV antibody level; and 2) questions relating to cord serum RSV antibody level are addressed in a subpopulation using a case-control study design.

## MATERIALS AND METHODS

### Total population study

The study population consists of 1,179 healthy infants, enrolled at birth into the Tucson Children's Respiratory Study between May 1980 and January 1984, and includes illnesses observed until December 1985. Eligible participants were those who planned to use the pediatricians of the largest local health maintenance organization in Tucson. This number (1,179) represents those who were followed by the health maintenance organization pediatricians during all or part of their first year of life. Children were given a follow-up time of 12 months if parents stated they still used the health maintenance organization pediatricians on a follow-up questionnaire completed in the child's second year of life ( $1.6 \pm 0.35$  (mean  $\pm$  standard deviation) years), or if the child was seen for a "well-baby" visit between 12 and 15 months. Other children are assigned a follow-up time based on their age at their last recorded well-baby visit.

All LRIs were diagnosed by the pediatricians, at the time of the office visits for the illnesses, according to criteria agreed upon by the pediatricians and the investigators (17). Nasopharyngeal and throat specimens were collected at the time of the LRI for viral cultures and for examination by immunofluorescent techniques to detect the presence of RSV and other viruses (18). An episode was considered to be RSV positive if either culture, immunofluorescence, or both were positive.

Information concerning duration of breast feeding in the first year of life was derived from a combination of data from two sources: prospectively from well-baby visits and retrospectively from questionnaires completed by parents when enrollees were in the second year of life (19, 20). There was excellent concordance (90 percent) between the two sources. Priority was given to the prospective data that were used for 72 percent (705/982) of those with information from either source. There were 197 (16.7 percent) infants with insufficient or no information from either source. Duration of breast feeding from both sources was grouped into the following categories: none, <1 month, 1–3 months, 4–6 months, and >6 months.

Exclusive breast feeding was distinguished from breast feeding in combination with milk and/or formula using the following categories derived from questions asked prospectively at the 2-month well-baby visit: breast feeding only at 2 months, breast feeding plus formula at 2 months, and no breast feeding at 2 months (milk or formula only). Similar variables were derived from information collected at the 4-, 6-, 9-, and 12-month well-baby visits. Information on other factors considered in this analysis came from questionnaires completed by the parents at enrollment: maternal education ( $\leq 12$  years,  $>12$  and  $\leq 16$  years, and  $>16$  years); the number of persons sharing the same bedroom as the child (none, one, and two or more persons); birth month (December to February, March to May, June to August, and September to November); sex; maternal ethnicity (Anglo and others); and

maternal smoking. Information obtained in the second year of life questionnaire as to whether or not a child spent  $\geq 9$  hours per week in day care was also considered.

**Statistical analysis.** The percentage of RSV-positive LRIs with respect to all LRIs studied virologically was calculated for each month during the entire study period (from May 1980 to December 1985). Data from those months during the study period when RSV was isolated were used for subsequent analysis. Since RSV occurs in epidemics, these were the months when infants were considered at risk for RSV-LRIs. During these months, the appropriate status was assigned to each subject for each month of age in the first year of life, within a subject's follow-up period, e.g., RSV-positive LRI, RSV-negative LRI, no RSV virologic study done, or no LRI. Only the first RSV-LRI episode was considered, and subjects were excluded from analyses in subsequent months following a RSV-LRI. For calculating incidence measures, RSV-negative LRIs and those for which no virologic data were obtained were ultimately combined with cases with no LRI. If any of these cases are misclassified, the resulting bias would be toward the null hypothesis of no effect. There were 31 LRIs with no virologic information, including three in the 1- to <3-month age range; removing these from analyses did not affect the results. In addition, 56 infants were excluded as their follow-up times in the first year of life did not include a RSV season.

Two parameters were derived from the data. 1) Person-time incidence rates (21) expressed the rate of first RSV-associated LRIs per 1,000 person-months at risk, cumulated by month of age both overall and for factors of interest. The following equation calculates the person-time incidence rate at month  $m$ , where  $m$  is from 1 to 12 months.

$$\text{Rate at month } m = \frac{\text{no. of RSV-LRIs (0-}m\text{ months)}}{\text{no. of person-months (0-}m\text{ months)}} \times 1,000$$

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This measure gives an overall cumulated rate per 1,000 per month up to each month of age in the first year of life. Plots show this rate on the ordinate. 2) Incidence rates per 100 children at risk for RSV-LRIs were calculated for each month of age, both overall and for subcategories of the factors of interest, in order to evaluate effects by month of age in the first year of life.

These incidence measures may frequently be referred to as attack rates, since the population is at risk for RSV-LRIs only during the limited time period of the RSV epidemic (22).

The statistical significance of associations and trends between the various factors and the incidence by month of age was assessed bivariate using the  $\chi^2$  distribution with Yates' correction where appropriate. Relative risks (RRs) were computed as follows.

$$RR = \frac{\% \text{ with RSV-LRIs among those with risk factors}}{\% \text{ with RSV-LRIs among those without risk factors}}$$

Also calculated were 95 percent confidence intervals (CI). Kendall's tau (one-tailed) was used as a nonparametric measure of correlation or trend. Data were also evaluated in 2-month intervals, where rates were similar by month. Additionally, variables were combined to assess relative risks of a combination of risk factors. To assess multivariate effects, log-linear modeling was done using saturated models, and partial  $\chi^2$  statistics were computed to determine statistical significance of effects at an  $\alpha$ -level of 0.05. The partial  $\chi^2$  is the difference between the goodness-of-fit test statistic (likelihood-ratio  $\chi^2$ ) with and without the term or effect being tested. It also has a  $\chi^2$  distribution (one-tailed) and can be used to test the hypothesis that the effect is zero (23). Adjusted odds ratios (OR) were derived from the model coefficients.

#### RSV antibody case-control study

The case-control study was limited to the larger group of infants of Anglo maternal ethnicity. RSV-positive LRIs were identified

in 135 infants with follow-up times of 1 year; 94 of these were of Anglo maternal ethnicity. The latter were matched with Anglo infants for sex, and month of birth with infants who were also followed for the entire first year, but with no LRI. Cord sera were available on 86 matched pairs of Anglo infants who also had breast feeding information.

The level of RSV antibody in cord sera was determined as previously described (24). Initial 1:10 serum dilutions were prepared in phosphate-buffered saline with subsequent 1:20–1:640 serial dilutions. Sera were overlaid onto wells containing RSV-infected and -uninfected, acetone-fixed cells and incubated at 35–37°C for 30 minutes. Wells were washed twice for 5 minutes in phosphate-buffered saline and then overlaid with appropriately diluted fluorescein isothiocyanate-conjugated goat anti-human immunoglobulin G (heavy and light chain specific). They were incubated at 35–37°C for 30 minutes and subsequently washed twice in phosphate-buffered saline. Buffered glycerol was used as the mounting medium, and wells were examined with a Zeiss epifluorescence microscope for specific granular cytoplasmic fluorescence  $\geq 1+$  in intensity to determine the end-point dilution.

**Statistical analysis.** Odds ratios were calculated both for single factors and while controlling for other factors by stratification. Mantel-Haenszel estimates of adjusted odds ratios and 95 percent confidence intervals were calculated (25). Logistic regression was also performed to provide odds ratios while controlling for other risk factors.

All statistical analysis used SPSSX or SPSS-PC software and custom programs.

## RESULTS

### Total population study

Of a total of 460 LRIs in the first year of life, 12 (2.6 percent) required the infant to be hospitalized, and 375 (82 percent) had virologic studies. There were 148 (39.5 percent) episodes positive for RSV, including five repeat RSV infections that were excluded from analysis. Of the 143 remaining RSV-positive LRIs, 123 (86 percent) were

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diagnosed as bronchiolitis, and 121 (84.6 percent) were associated with wheezing on examination, the majority (94 percent) of which were bronchiolitis. Information from a nurse-administered parental questionnaire at a convalescent visit indicated that the duration of illnesses ranged from <1 week (7 percent) to >3 weeks (18 percent), with a maximum frequency of 32 percent of illnesses lasting 7–10 days. Two cases diagnosed as bronchiolitis were hospitalized. In addition, there were 67 other LRIs associated with wheezing but not with RSV. Of the 375 LRIs studied virologically, RSV was detected most often with 39.5 percent, followed by parainfluenza virus type 3 in 34 (9 percent) instances, none of which was a repeat infection; detection rates were 1–5 percent for the other viruses assayed (parainfluenza virus types 1 and 2, influenza virus types A and B, adenoviruses, enteroviruses, cytomegalovirus, and rhinovirus).

The monthly distribution of the percentage of positive RSV results among all LRIs studied virologically for children <1 year of age was similar for each study year. Study years were combined, therefore, and figure 1 shows the combined distribution by month for the study years 1980–1985. RSV is clearly epidemic in nature, occurring from October to April and peaking in January. This distribution compares well with that for

positive RSV results among all LRIs ( $n = 1,052$ ) diagnosed in the study until October 1986 (17).

Table 1 indicates the distribution of the study population by the various risk factor categories of interest considered in this analysis. Not all subjects had complete sets of information. There were a number of significant relations within this set of variables. Infants who were breast-fed the longest were more likely to have Anglo non-smoking mothers with more education, to have fewer persons sharing the bedroom, and to be less likely in day care ( $p < 0.005$ , adjusted for multiple comparisons). Neither birth month nor sex was associated with any other risk factor considered in this analysis.

*Incidence rate per 100 infants by month.* The incidence of RSV-LRIs per 100 infants by month of age (figure 2) is fairly constant during the 3- to 7-month age range at 3.7–4.0 per 100 infants at risk each month, after which it decreases. No RSV-LRIs were observed before 1 month of age. Rates were similar in the 2-month intervals after 1 month of age, and subsequent analysis of incidence rates per 100 children combined data into 2-month intervals as follows: 1–<3 months, 3–<5 months, 5–<7 months, 7–<9 months, and a final interval of 9–<12 months. Two RSV-LRIs identified at 12 months are excluded.

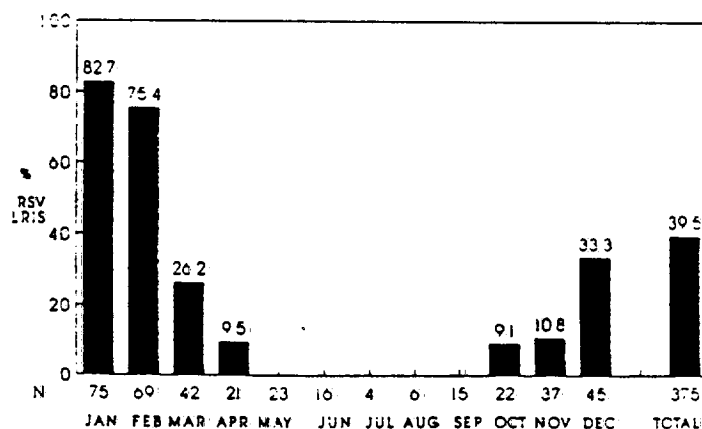


FIGURE 1. Positive respiratory syncytial virus results by percentage among all lower respiratory tract illnesses studied virologically by month in a health maintenance organization study population, Tucson, Arizona (1980–1985). RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; N, number of cases.

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TABLE 1. Distribution of factors considered in a health maintenance organization study population, Tucson, Arizona, 1980-1985

Variable	No.	%
Duration of breast feeding		
None	157	13
<1 month	53	4
1-3 months	235	20
4-6 months	152	13
>6 months	385	33
Missing information	197	17
Exclusivity of breast feeding at 2 months		
Exclusively breast-fed	458	39
Breast + formula	236	20
No breast feeding	335	28
Missing information	150	13
Maternal education		
≤12 years	375	32
>12-≤16 years	593	50
>16 years	206	18
Missing information	5	<1
No. sharing same room		
None	689	58
One	299	25
Two or more	167	14
Missing information	24	2
Birth month		
January-March	198	17
April-June	289	24
July-September	366	31
October-December	326	28
Sex		
Male	575	49
Female	601	51
Missing information	3	<1
Ethnicity		
Anglo	874	74
Hispanic	221	19
Other	81	7
Missing information	3	<1
Maternal smoking		
Yes	204	17
No	972	82
Missing information	3	<1
Day care		
Yes	467	40
No	532	45
Missing information	180	15
Total	1,179	100

Table 2 shows univariate relations between the risk factors considered and the incidence of RSV-LRIs per 100 children between the ages of 1 and <3 months. (Rel-

ative risks are included as risk ratios with confidence intervals.) For breast-feeding status, RSV-LRI rates were similar in the categories of <1 month and no breast feeding (4.7 percent and 6.9 percent, respectively), which were combined into one category called "minimal" breast feeding. The relative risk of RSV-LRIs associated with minimal breast feeding at this age was 2.5. In addition, the relative risk increased from 2.2 for those who were breast-fed and also given formula to 4.0 for those given formula or milk only, when compared with those who were exclusively breast-fed at 2 months of age, with a statistically significant trend ( $p = 0.01$ ). Similar trends of borderline significance were observed when considering RSV-LRIs at 1-<2 months and 2-<3 months of age.

No other significant protective effects of breast feeding were observed at any other age up through 12 months. (The RRs for having a RSV-LRI with minimal breast feeding for other age intervals were as follows: 3-<5 months,  $RR = 0.9$ ; 5-<7 months,  $RR = 0.7$ ; 7-<9 months,  $RR = 1.2$ ; 9-<12 months,  $RR = 0.33$ .) Breast feeding at the time coincident with the month of age being analyzed also showed no additional protective effect.

Several factors other than breast feeding are also significantly related to the incidence of RSV-LRIs in the first year of life. Infants of mothers with a high school education or less had a higher incidence (5.3 percent) of RSV-LRIs between 1 and <3 months compared with 1.7 percent in the infants of mothers with more education (table 2). There was no significant difference in the incidence of RSV-LRIs when comparing infants of mothers with 12-16 years and >16 years of education. No significant trends associated with maternal education were observed beyond 3 months of age.

The incidence of RSV-LRIs per 100 children between 1 and <3 months was significantly higher in males (4.3 percent) compared with females (1.3 percent) (table 2). However, this effect was predominantly due to Hispanic males; 44 percent of 16 infants between 1 and <3 months of age with RSV-

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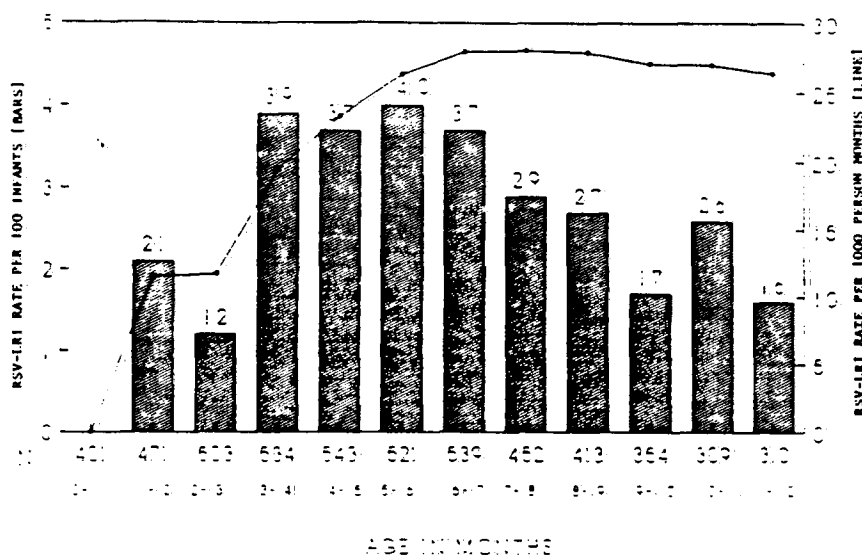


FIGURE 2. Rates of respiratory syncytial virus-associated lower respiratory tract illnesses in the first year of life, in a health maintenance organization study population, Tucson, Arizona (1980-1985). RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; N, number of cases. (For rates above, see Materials and Methods for calculation.)

LRIs were Hispanic males; none was an Hispanic female. This also accounts for the significantly higher incidence of RSV-LRIs between 1 and <3 months of age among infants of Hispanic origin compared with Anglos (table 2). No consistent trends were observed beyond this age in the relation of RSV-LRIs to sex or ethnicity.

There was a significant increase in the RSV-LRI incidence in association with increasing numbers of others sharing the same bedroom with the child from 1-5 months of age, with trends of borderline significance from 6 to 12 months. Table 2 shows a significant trend for rates between 1 and <3 months of age, with a relative risk of 1.6 for one person sharing and 4.7 for two or more persons sharing compared with none sharing. At 3-<5 months, the equivalent relative risks are 3.9 and 6.1, again with a significant trend ( $p < 0.002$ ).

Between 7 and <9 months of age, those in day care had an incidence rate of RSV-LRIs of 6.7 per 100 children versus 2.4 for those not in day care ( $\chi^2 = 4.4$ ,  $p = 0.04$ ). Between 9 and <12 months, the same trends were seen, but they were of borderline statistical significance. No significant trends re-

lating day care to RSV-LRIs were seen below 7 months of age.

Maternal smoking was not related to the incidence of RSV-LRIs at any age in the first year of life.

**Incidence rate per 1,000 person-months.** The cumulated rate of RSV-LRIs per 1,000 person-months, from 1-12 months of age, is superimposed on figure 2. This rate is low in the first few months (12/1,000 person-months), increases until 6 months of age (26/1,000 person-months), and then levels off. This cumulated measure acts as a smoothing function in that it reduces the amount of variation or fluctuations present in the data by month. Although the incidence per 100 children is fairly constant between 3 and 7 months, the person-time incidence rate (per 1,000 person-months) increases until 7 months, since it is constrained by the low initial rate, and increases as successive RSV-LRI occurrences and person-months are added. After 6-7 months, the cumulated measure levels off as the incidence per 100 children by month decreases. The person-time incidence rate of RSV-LRIs for the entire first year of life is 26.4 per 1,000 infants per month.

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TABLE 2. Single-factor relations with RSV-LRI† between 1 and &lt;3 months of age, in a health maintenance organization study population, Tucson, Arizona, 1980–1985

Variable	No.	RSV-LRIs (%)‡	RR†	p value (Kendall's tau)
Breast feeding				
None-<1 month	114	5.3	2.5 (0.9–7.0)‡	0.04
1 month or more	380	2.1		
Amount of breast feeding at 2 months				
Formula and/or milk	177	5.1*	4.0 (1.1–14.1)	0.01
Breast + formula	105	2.9		
Exclusively breast-fed	234	1.3		
Maternal education				
≤12 years	170	5.3	3.1 (1.2–8.2)	0.01
>12 years	409	1.7		
Sex				
Male	280	4.3	3.2 (1.0–9.8)	0.02
Female	297	1.3		
Ethnicity				
Hispanic and other	148	4.7	2.3 (0.9–6.0)	0.05
Anglo	431	2.1		
No. sharing child's room				
Two or more	74	8.1**	4.7 (1.6–14.2)	0.001
One	147	2.7		
None	349	1.7		
Maternal smoking				
Yes	108	2.8	1.0 (0.3–3.5)	NS
No	471	2.8		

\* Trend  $p = 0.01$ ; \*\* trend  $p = 0.007$ 

† RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; RR, relative risk (ratio) (percentage with RSV-LRIs among those with risk factor/percentage with RSV-LRIs among those without risk factor); NS, not significant.

‡ Numbers in parentheses, 95% confidence interval.

Figure 3 indicates the rates of RSV-LRIs per 1,000 person-months differentiated by the duration of breast feeding in three categories (minimal, 1–6 months, >6 months). Through 5 months of age, those who receive minimal breast feeding appear more likely to have RSV-LRIs than those who are breast-fed longer. After 5 months of age, there appears to be little or no protective effect. These trends are statistically significant using the  $\chi^2$  distribution ( $p < 0.05$ ) at 1–<2 months only and of borderline significance between 1 and <3 months of age when considering minimal breast feeding versus other categories combined. The use of different category combinations (including none, <1-month, and 1- to 3-month breast feeding) confirmed that the significant difference was consistently between minimal and >1-month breast feeding in the 1- to

<3-month age range, consistent with the analysis of the incidence per 100 infants by month of age.

Figure 4 illustrates how the incidence rate per 1,000 person-months (person-time incidence rate) varies by month of age according to birth month. The distribution of incidence rates is displaced along the x-axis, depending on when a child was born in relation to the RSV season. For those born in the first half of the RSV season (from October to December), the rate increases until 5 to 6 months of age, whereas the rate for those born in the latter half of the RSV season remains fairly constant until the next RSV season is encountered. The distributions of those born 1–3 and 3–6 months prior to the RSV season are displaced along the x-axis accordingly.

Considering the entire first year of life, the

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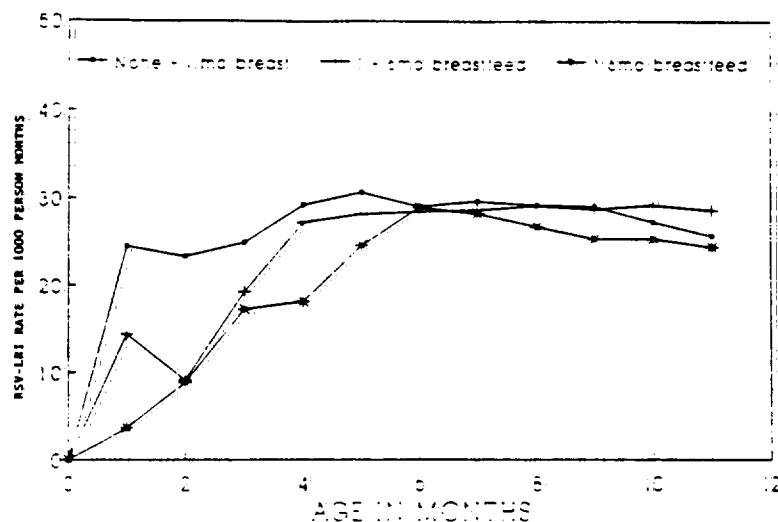


FIGURE 3. Person-time incidence rates of respiratory syncytial virus-associated lower respiratory tract illnesses up to 12 months of age by breast feeding, in a health maintenance organization study population, Tucson, Arizona (1980-1985). RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness. (See Materials and Methods for calculation of person-time incidence rates.)

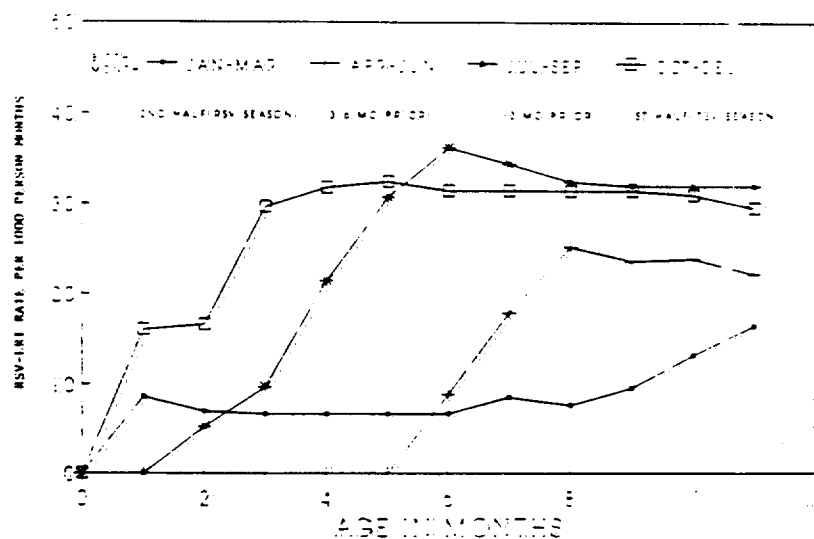


FIGURE 4. Person-time incidence rates of respiratory syncytial virus-associated lower respiratory tract illnesses up to 12 months of age by birth month in a health maintenance organization study population, Tucson, Arizona (1980-1985). RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; mo, month. (See Materials and Methods for calculation of person-time incidence rates.)

incidence of RSV-LRIs was 16.7 for those born from July to September and 15.6 for those born from October to December, compared with 9.5 and 11.7 for birth months

January-March and April-June, respectively. Combining these categories gives an incidence of 16.2 percent for those born from July to December, which is signifi-

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cantly different from the incidence of 10.8 percent for those born from January to June ( $\chi^2 = 5.16$ ;  $p < 0.02$ ).

**Multivariate analysis.** Variables considered for multivariate analysis were those that had shown some statistically significant association with the incidence of RSV-LRIs and an elevated relative risk during each 2-month age interval. Variables included were the following: duration (minimal versus >1 month) and exclusivity of breast feeding (breast only, breast plus formula, formula/milk only at 2 months); maternal education; number sharing the child's room; sex; and ethnicity. (Maternal smoking showed no significant contribution to multivariate analysis when investigated.) Day care was included in analyses after 7 months of age. All variables were collapsed into dichotomous categories (except the exclusive breast-feeding variable) as follows: maternal education,  $\leq 12$  years versus >12 years; none/one sharing the room versus two or more; Anglo versus Hispanic and other ethnicities. For each 2-month age interval, log-linear analysis was used to assess relations between RSV-LRIs and other risk factors.

At 1–<3 months of age, relations between RSV-LRIs, exclusivity of breast feeding, and

other risk factors were evaluated. No direct effect remained for exclusivity of breast feeding after controlling for all other variables. However, there was a significant interaction between the incidence of RSV-LRIs, years of maternal education, and exclusivity of breast feeding (partial  $\chi^2$ ,  $p < 0.01$ ), after accounting for all other effects. This interaction is shown in figure 5. It is apparent, although cell sizes are small, that in the lower maternal education category, there is a significant increasing trend in the incidence of RSV-LRIs between 1 and <3 months of age, from exclusively breast-fed infants (0.0 percent) to breast- and formula-fed infants (3.3 percent) to those fed formula or milk only (9.6 percent) ( $\text{tau } p = 0.02$ ). The odds ratio for having a RSV-LRI in those infants of mothers with a low educational level who were not breast-fed was 6.8 (95 percent CI 0.8–56.0). This effect was seen with trends of borderline significance in Anglo males and females and in Hispanic males, although numbers are small; there are no RSV-LRIs in Hispanic females in this age range. There is no such association in the higher maternal education category. An equivalent analysis substituting duration for exclusivity of breast feeding gave similar results.

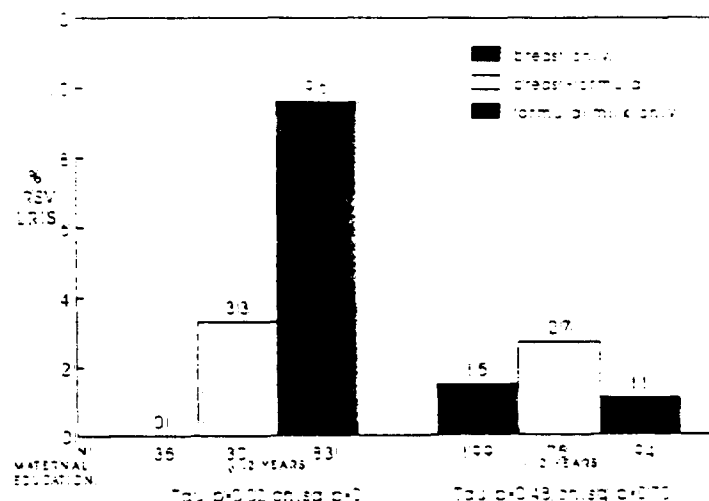


FIGURE 5. Incidence rates of respiratory syncytial virus-associated lower respiratory tract illnesses between 1 and <3 months of age by maternal education and breast-feeding status, in a health maintenance organization study population, Tucson, Arizona (1980–1985). RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; N, number of cases.

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After accounting for all other interactions and effects at 1- to <3 months of age, significant direct effects remained only for sex (partial  $\chi^2$ ,  $p = 0.04$ ) (OR = 1.6; 95 percent CI 0.7-3.7) and for number sharing the child's room (partial  $\chi^2$ ,  $p = 0.03$ ) (OR = 5.3; 95 percent CI 2.3-12.2). The bivariate relation seen between RSV-LRIs and ethnicity at this age was not significant after controlling for other effects, mainly because it is observed as an interaction among RSV-LRIs, sex, and ethnicity (partial  $\chi^2$ ,  $p < 0.03$ ).

Table 3 shows different combinations of three risk factors (two or more sharing the child's room, low maternal education, and minimal breast feeding) assessed in relation to RSV-LRIs. The relative risk of having a RSV-LRI increases from 4.0 for those who had two or more persons sharing their room, to 5.6 for those who also have a low maternal education, to 8.0 when little or no breast feeding is included; all combinations are highly significant. Similar relations were observed in both males and females and for both ethnic groups, although the trends did not always reach statistical significance.

Log-linear analyses performed for other 2-

month age intervals showed that direct effects persisted only for sharing the room with two or more people in the 3- to <5-month age range (OR = 3.7; 95 percent CI 1.6-8.7; partial  $\chi^2$ ,  $p < 0.01$ ) and a smaller effect for day care in the 7- to <9-month age range (OR = 1.4; 95 percent CI 0.7-2.9; partial  $\chi^2$ ,  $p < 0.03$ ), after controlling for other variables and effects.

#### RSV antibody case-control study

The cord serum RSV antibody titer in the 86 matched pairs ranged from <10 (undetectable) to 2,560. The distribution was positively skewed (3.6) with a median value of 80. A  $\log_{10}$  transformation (assigning the value of 5 to undetectable titers) reduced the skew to 0.06, giving a geometric mean of 117 (standard deviation, 3.5). Because of its distribution, the cord serum RSV antibody titer was considered as a categorical variable, initially in four categories: 0-20, 40-80, 160-320, and  $\geq 640$ . There was a distinct drop in the percentage of RSV-LRIs in the last two categories. Subsequently, two categories were used for analysis: 0-80 (low-titer group) and  $\geq 160$  (high-titer group), which

TABLE 3. Multivariable relations with RSV-LRIs\* between 1 and <3 months of age, in a health maintenance organization study population, Tucson, Arizona, 1980-1985

Variable	No.	RSV-LRIs (%)	RR*	p value (Kendall's tau)
Two or more sharing room	74	8.1	4.0 (1.5-10.7)†	0.002
None or one sharing room	476	2.0		
Two or more sharing room and maternal education $\leq 12$ years	43	11.6	5.6 (2.0-15.3)	0.0001
All other combinations of sharing and maternal education	527	2.1		
Two or more sharing room, maternal education $\leq 12$ years, and minimal breast feeding	21	19.0	8.0 (2.8-22.8)	0.00001
All other combinations of sharing, maternal education, and feeding	505	2.4		

\* RSV-LRI, respiratory syncytial virus-associated lower respiratory tract illness; RR, relative risk (ratio) (percentage with RSV-LRIs among those with risk factors/percentage with RSV-LRIs among those without risk factors).

† Numbers in parentheses, 95% confidence interval.

divides the distribution approximately at the median.

In the first year of life, the percentage of RSV-LRIs in those with a low cord serum RSV antibody titer was 56.3 compared with 44 percent in the high-titer group, with an OR for having a RSV-LRI with lower cord serum RSV antibody levels of 1.67 (95 percent CI 0.9–3.1;  $\chi^2$ ,  $p = 0.13$ ). Similar trends were seen in the 57 matched pairs <7 months of age (55 percent vs. 43 percent; OR = 1.66; 95 percent CI 0.8–3.5) and in the 22 matched pairs from 7 to 12 months of age (59 percent vs. 44 percent; OR = 1.81; 95 percent CI 0.6–5.3). Stratifying and adjusting for breast feeding gave a Mantel-Haenszel odds ratio of 1.6 (95 percent CI 0.9–3.0;  $\chi^2$ ,  $p < 0.1$ ). Stratifying and adjusting for maternal education also gave an odds ratio for having a RSV-LRI with lower cord serum RSV antibody of 1.6 (95 percent CI 0.9–3.0;  $\chi^2$ ,  $p < 0.1$ ) with no evidence of interaction.

However, a combination of three risk factor categories, i.e., lower cord serum RSV antibody, lower maternal education, and minimal breast feeding, gave an increased odds ratio of 4.4 (95 percent CI 1.1–18.3;  $\chi^2$ ,  $p < 0.05$ ), compared with infants in the reference group who were breast-fed, had higher cord serum RSV antibody, and had higher maternal education. All other combinations of risk factor categories gave an odds ratio of 1.6 (95 percent CI 0.8–3.2;  $\chi^2$ ,  $p < 0.25$ ), compared with the reference group.

Using logistic regression to assess the relation between RSV-LRIs and antibody level while controlling for maternal education and breast-feeding status gave an odds ratio for having a RSV-LRI with a low antibody level of 1.6 (95 percent CI 0.8–2.9;  $p < 0.1$ ). Low maternal education was associated with an odds ratio for having a RSV-LRI of 2.5 (95 percent CI 1.2–5.2;  $p < 0.01$ ). Breast feeding was not a significant contributor to this model, and no additional risk associated with an interaction between low cord serum RSV antibody and minimal breast feeding was demonstrated.

Since cases were matched with controls

for birth month and sex, there was no relation between these factors and RSV-LRIs in this case-control subgroup. However, those born from January to June were more likely to have a higher cord serum RSV antibody titer (>80) than were those born from July to December (64 percent vs. 42 percent;  $\chi^2$ ,  $p = 0.01$ ). There was no statistically significant relation between age at the time of the RSV-LRI and the level of cord serum RSV antibody.

Of the 86 matched pairs, 25 matches were in the age range of <5 months, which provided an adequate number to analyze, at least bivariate. In this younger age range, there was no association between RSV-LRIs and RSV antibody level (OR = 1.0; 95 percent CI 0.3–3.0;  $\chi^2$ ,  $p = 1.0$ ). However, the odds ratio for having a RSV-LRI with minimal breast feeding was 5.4 (95 percent CI 1.0–28.8;  $\chi^2$ ,  $p = 0.08$ ). The relation between having a RSV-LRI and low maternal education had an odds ratio of 2.7 (95 percent CI 0.8–9.5;  $\chi^2$ ,  $p = 0.2$ ). When both breast-feeding status and cord serum RSV antibody were considered, 100 percent (6/6) of those with lower cord serum RSV antibody, who were minimally breast-fed, had RSV-LRIs, compared with 35 percent (7/20) of those with lower cord blood RSV antibody who were breast-fed. (The OR is undefined as all cases who were minimally breast-fed had RSV-LRIs;  $\chi^2$ ,  $p = 0.02$ .) Conversely, there was no significant association between breast-feeding status and RSV-LRIs in those with higher cord serum RSV antibody (OR = 1.0; 95 percent CI 0.1–8.6;  $\chi^2$ ,  $p = 1.0$ ).

## DISCUSSION

A statistically significant protective effect of breast feeding against RSV-LRIs has been observed in this population. As in other studies (6, 9), it is relatively subtle and best demonstrated in those with lower socioeconomic status. The effect in its simplest bivariate mode is seen during the first few months of life only; this is demonstrated in both the larger survey sample and the case-control study. However, the independent significance of breast feeding does not with-

stand controlling for other implicated factors (number sharing child's room, maternal education, sex); it remains statistically significant as an interaction with maternal education. Infants of mothers with a high school education or less appear to be protected against having RSV-LRIs by breast feeding in general and more so by exclusive breast feeding, but significantly only up to 3 months of age.

Others have documented the importance of the level of maternal education as a risk factor for infections (26). Although the latter study showed only marginal significance of a protective breast-feeding effect in those with 12 years of education and a nonsignificant trend in those with <12 years, the lack of any protective effect in those with  $\geq 13$  years of education is consistent with our findings.

The number of others sharing the same room with the index child, as a measure of crowding, was clearly an important risk factor for RSV-LRIs, especially when there were two or more sharing. In addition, the risk increased with a combination of lower socioeconomic status conditions plus minimal breast feeding. In other studies, various indices of crowding have been shown to be important in RSV infections (4) and in acute bronchiolitis (27, 28). The number of siblings has been shown to have an impact on infection and LRIs (10, 27-29). Although we have not considered separately the number of siblings as a risk factor, it was highly correlated with the number of persons sharing the child's room.

The case-control study shows a small protective effect against RSV-LRIs for those infants having higher cord serum RSV antibody titers, compared with those with lower levels. Those with lower cord serum RSV antibody titers, who also had minimal breast feeding, were especially at high risk for a RSV-LRI in the first few months of life. The smaller number of cases in the case-control study limits the number of risk factors that can be considered. However, it is clear that combinations of risk factors which include lower cord RSV antibody increase the likelihood of a child having a RSV-LRI. The

relative risk of having a RSV-LRI increased from 1.6 for those with lower cord serum RSV antibody to 2.2 for those who also had minimal breast feeding to 4.4 for those who, in addition, had a lower maternal education. We find no evidence to support the hypothesis (12, 16) that a higher cord serum RSV antibody titer may increase susceptibility to RSV-LRIs.

In developing nations, the evidence for a protective effect of breast feeding is thought to be more conclusive (8, 30). It seems likely that any protective effect of breast feeding demonstrated in the more developed nations would be observed mainly in those segments of the community where infection would be more probable, e.g., as found in the present study, in conditions of lower socioeconomic status (measured here by maternal education and/or crowding), which may approximate those of the less developed world. Wright et al. (19) have shown in this same population a protective effect of breast feeding in relation to early wheezing LRIs, especially in crowded conditions.

It is plausible to speculate that there may be several effects of breast feeding on the lung. There may be an effect on lung development (31), possibly mediated by growth factors (32-34). Also, there may be additional immunologic benefits of breast feeding. There is also the possibility that the act of breast feeding itself limits the chances of infection by reducing the number of persons who have regular contact with a young infant.

Two potential mechanisms of protection have been demonstrated. 1) This and other studies relate infant RSV antibody levels inversely to various aspects of RSV infection, including severity and age (3, 11). 2) Human colostrum has been shown to contain neutralizing activity (partly immunoglobulin A) against RSV in vitro (5, 15). However, the method of acquiring antibody as well as its mode of action may not necessarily involve breast feeding. This study shows no additional protection associated with breast feeding against RSV-LRIs in those who already have a higher cord serum RSV antibody level, compared with a pro-

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protective effect of breast feeding in those with lower cord blood titers. The nature of this effect is speculative and may or may not involve passively acquired antibody from breast milk. Cell sizes for these analyses are, however, very small. Interestingly, some have suggested that, since infants have been shown through radiologic studies to aspirate milk during feeding, the immunoglobulin A localized in the respiratory tract might protect against severe respiratory infection (5).

Considering birth month, Carlsen et al. (27) have shown that those born during the summer months who were approximately 6 months old at the time of the RSV outbreak were most at risk for RSV bronchiolitis. Our analysis is consistent with this finding, since the highest incidence rate (per 100 children) over the entire first year was found for those born between July and September. Glezen et al. (3) have also shown a three times greater risk of RSV infection for infants born during the 6-month period ending with the peak of the epidemic. In the Children's Respiratory Study population, the relative risk of having a RSV-LRI in the first year of life if born between July and December was 1.5 times more than for those born from January to June. In addition, the cord serum RSV antibody titer was significantly lower for those born between July and December, compared with those born between January and June.

The epidemic nature of RSV as observed in other studies (35) was confirmed in this population. The simple incidence rate for RSV-LRIs in this population was 12 per 100 children in the first year of life, considerably higher than the infection rate of 3 per 100 children per year up to 2 years of age observed by Glezen et al. (35). (The incidence for parainfluenza virus type 3 LRIs in this population (data not shown) was comparable at 2.9 to the 2 per 100 children observed by Glezen et al. (35).) Advances made in laboratory techniques over the past decade and our surveillance method probably account for many of the discrepancies between the studies. In the Children's Respiratory Study, cultures for viruses have been positive in >60 percent of the LRIs

cultured. This is nearly two times greater than the isolation rates reported in earlier studies (18).

Others (1, 36) have commented on the "relative sparing" of infants of  $\leq 1$  month of age from RSV bronchiolitis. This phenomenon was seen also in the Children's Respiratory Study population: no RSV-LRIs were observed up to <1 month of age and relatively few up to <3 months of age. Parrott et al. (36) found that the frequency of RSV infection did not vary widely with age between 1 and 18 months in those whose respiratory illness did not require hospitalization, with a maximum frequency of RSV infection at 2 months of age. In contrast, among those who were hospitalized, there was a distinct peak at 2 months of age. In this study, the peak incidence of RSV-LRIs is between 3 and 6 months of age. Clearly different populations have different age distributions of RSV-LRIs. It is interesting and provocative to note that the rate of breast feeding in the US population, both exclusive and supplemented with formula, has increased from 1955 to 1982 (37). Breast-feeding rates were considerably lower in the early 1970s (13.9 percent at 2 months of age in 1971) than in the 1980s (47.5 percent at 2 months in 1984) (37). The latter compares with 59 percent breast feeding at age 2 months in the Children's Respiratory Study population. This increase in breast-feeding rates could explain the later peak incidence of RSV-LRIs in the Children's Respiratory Study population in the 1980s compared with the outpatient results of Parrott et al. (36) in the 1970s.

In this population, it appears that males are more susceptible to RSV-LRIs in the early months of life; this effect was predominantly in Hispanic males. Other epidemiologic studies have shown that males are more likely than females to have RSV-LRIs up to 5 years of age (35), to be hospitalized (36), or to have more severe infections (3). Additionally, Glezen et al. (3) have observed a possible excess of infants of Hispanic origin hospitalized with RSV infections. In this study, it seems that the increased risk for RSV-LRIs associated with ethnicity was en-

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tirely due to increased RSV-LRIs in Hispanic males. This phenomenon deserves further investigation.

There may be some anatomic reasons why males have more lower respiratory tract symptomatology with RSV infections. As we have previously shown (31), low lung function predates the onset of wheezing LRIs, suggesting that infants who are born with smaller airways may be at greater risk for airway obstruction and increased respiratory symptomatology with a viral infection. We have also previously demonstrated that males are more likely to have smaller airways for their lung size than females (38). This potentially could put them at increased risk for symptomatology with viral infections. This would clearly be of more clinical importance in the first few months after birth before considerable growth has occurred.

The findings in other studies of associations between day care and increased LRIs (10, 27) are confirmed in this population for RSV-LRIs. The increase in relation to day care was observed, however, only between 7 and <9 months of age. The effect at this age also withstands controlling for other confounders. It seems plausible that the effect of day care was seen at this time because infants are more likely to be in day care after 6 months. Retrospective collection of more detailed day-care information, including age at the time of care, is currently in progress, and its analysis will be the subject of future investigations.

Regarding maternal smoking, no effect of any significance on RSV-LRIs has been demonstrated in this analysis, particularly in the early months of life. Carlsen et al. (27) also showed no effect of parental smoking in infants hospitalized with acute bronchiolitis compared with controls, although smoking rates of all parents were high. Others, however, have demonstrated a highly significant relation between parental smoking and LRIs in a community population (29), bronchiolitis in a nonhospitalized case-control study (28), and wheezing illnesses in atopic babies (39). A relation between maternal smoking, particularly  $\geq 20$  cigarettes per day,

and all LRIs (wheezing or nonwheezing) has been demonstrated in our study population for the first year of life (40). We have not examined quantity of cigarettes smoked in this month-by-month analysis because of smaller numbers.

Some studies have been criticized recently for lacking methodological standards to cope with sources of bias (41–43). Since enrollees in the Children's Respiratory Study planned to use the participating health maintenance organization which serves an employed population, extreme upper and lower socioeconomic status groups may be underrepresented, as discussed previously (17). However, we have also previously concluded that the illnesses observed in the first year of life are comparable to those described in other ambulatory populations, and appropriate surveillance methods have been used (18). A priori criteria were used to establish the presence of LRI, upon which information was collected prospectively. Also, information on feeding practices was collected prospectively and, although personnel recording such information were not blinded to any LRI outcome, this was only one of many factors considered in the Children's Respiratory Study. Some retrospective information was used, but there was excellent concordance between the prospective and retrospective data. Additionally, the data collected provided information on exclusive breast feeding. Multivariate analyses have also assessed effects while controlling for other factors and their interactions.

In summary, this prospective study in a large community population has demonstrated that a variety of factors appear to increase an infant's risk for having a RSV-LRI, especially in the early months of life. These factors could be categorized into two parts: 1) likelihood of exposure to infection, including crowding and low socioeconomic status, day care, and birth month; and 2) host susceptibility to infection, including lower cord serum RSV antibody levels, being male, and being minimally breast-fed. Clearly, there are other associations between variables and categories; for example, certain birth months are associated with higher

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cord serum RSV antibody levels. Combinations of factors greatly increase the risk of having a RSV-LRI. In addition, breast feeding appears to modify the risk of having a RSV-LRI and provides protection in conditions of lower socioeconomic status where exposure may be greater.

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Heumann, M., Foster, L.R., Johnson, L., and Kelly, L., "Human Health and Environmental Effects. Session 136. Woodsmoke Exposure and Human Health Impacts: Woodsmoke Air Pollution and Changes in Pulmonary Function Among Elementary School Children," Proc Annu Meet Exhib Air Waste Manage Assoc 15A(84): 1-15, 1991.

The authors of this study examined the possible relationship between exposure to woodsmoke and pulmonary function changes in 410 elementary school children in Oregon. The authors also considered the potential effects of ETS exposure. The authors reported that "children in homes heated by woodstoves showed greater declines in FEV<sub>1.0</sub> than children in homes that did not use woodstove heat." The reported association appeared among children living in both high and low outdoor air pollution exposure areas. Children exposed to ETS at the time of the baseline spirometry measurements had "markedly lower lung function measurements" than children who were unexposed. The authors stated that "children not exposed to tobacco smoke had significant declines in lung function measurements during the period of increased ambient PM pollution levels" and that "their mean FEV<sub>1.0</sub> levels dropped to those of the children who were exposed to tobacco smoke."

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**Woodsmoke Air Pollution and Changes in  
Pulmonary Function Among Elementary  
School Children**

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## INTRODUCTION

Klamath Falls, a Southern Oregon community with a population of 37,500, has had recurrent episodes of elevated air pollution levels due to respirable particulate matter ( $PM_{10}$ ). These air pollution episodes have occurred in winter months, during periods of air stagnation, temperature inversion, and heavy use of woodstoves for home heating.

$PM_{10}$  level data for a three year period, shown in Figure 1, reveal violations U.S. Environmental Protection Agency's National Ambient Air Quality Standards (NAAQS) during the winter heating season. Some of the nation's highest  $PM_{10}$  pollution levels have been recorded in this community. Woodsmoke from home heating with woodstoves accounts for an estimated 64.6% of the annual  $PM_{10}$  emissions in the Klamath Falls Air Quality Control Area<sup>1</sup>. During winter worst day emissions, wood smoke may account for 81% of the  $PM_{10}$  pollution.

$PM_{10}$  air pollution tends to concentrate in areas of the community corresponding to a geologic depression, which lies 65-90 feet below the average elevation of the city. Figure 2 shows the typical pattern of air pollution in Klamath Falls.

Local health authorities and the State Department of Environmental Quality have been monitoring the situation for a number of years. They have been coordinating efforts to reduce woodstove air emissions in this community through a program of voluntary curtailment of woodstove use during severe periods of air inversion. Because of concern about adverse health effects from woodstove smoke exposure to the residents of the community, the Oregon Health Division was asked to investigate this issue.

Several studies conducted in the United States and Europe have found an association between exposure to elevated levels of outdoor air pollution and increased frequency and rate of respiratory illness among school age children<sup>2-6</sup>. The Six Cities study of air pollution and health identified an association between particulate air pollution and reported rates of symptoms of illness including chronic cough, bronchitis, and chest illness<sup>7</sup>. However, this study did not demonstrate any significant change in lung function measures among the children studied. Measurable short-term declines in lung function were demonstrated in the Federal Republic of Germany and in Steubenville, Ohio, following air pollution episodes involving elevated total suspended particulates (TSP) and sulfur dioxide ( $SO_2$ ) levels<sup>8,9</sup>. Atmospheric  $PM_{10}$  levels were found to be strongly associated with hospital admissions for respiratory illness among children in one Utah county experiencing fine particulate pollution from a steel mill<sup>10</sup>.

Indoor heating with woodstoves has been linked with the occurrence of chronic respiratory symptoms in young children<sup>11</sup>. A variety of other indoor air pollutants have also been associated with increased rates of respiratory illness<sup>12</sup>.

## Methods

**Lung Function Measurement.** The Oregon Health Division designed a pilot study to measure seasonal changes in pulmonary function tests (PFT) among elementary school children in grades three through six. This age group has been shown to be acceptable for such study in similar investigations reported in the literature<sup>13,14</sup>. They are able to perform the spirometry maneuvers, and are easily accessible through local schools. Three area schools were chosen based on their proximity to high and low  $PM_{10}$  air pollution levels (see Figure 2). Peterson and Stearns Schools are located in the high exposure area. Conger School is located in a lower exposure area to the northwest of the geologic depression.

Parents of eligible school children were asked to enroll their child(ren) in the study. Participation was voluntary.

The pilot study used a repeated measures design in which PFT data were obtained on the same children at three points in time: Time-1, the baseline measurement, was conducted in October 1989, before the onset of the heating season; Measurements at Time-2 were obtained during the winter/heating season (March, 1990); Follow-up measurements (Time-3) were obtained after the end of the heating season (late May and early June, 1990).

The field technician team consisted of staff members of Klamath County Department of Health Services. They were trained to conduct the lung function measurements according to the American Thoracic Society (ATS) protocol<sup>10,11</sup>. Three ATS approved, Spiromate AS 600 computerized portable spirometers were used (Riko Medical Instruments)<sup>12</sup>. The spirometers were calibrated according to the manufacturers specifications<sup>13</sup>.

Pulmonary function testing followed ATS protocols for data quality and acceptability<sup>10,11</sup>. Children performed the spirometry maneuvers in a standing position. They did not wear nose clips. Each child had up to eight attempts to obtain at least three acceptable maneuvers. Values were corrected to body temperature and pressure, and fully saturated with water (BTPS). Standing height in stocking feet was recorded for each child at the time of testing.

PFT measurements included: forced expiratory volume at one second (FEV<sub>1</sub>) measured in liters; forced vital capacity (FVC), measured in liters; and peak expiratory flow (PEF), measured in liters per second. The ratio of FEV<sub>1</sub> to FVC (FEV<sub>1</sub>/FVC) was calculated from the data.

The technicians worked in parallel at each of the three schools. Children were randomly assigned to a technician for the baseline measurements. Each child was tested by the same technician on the same spirometer for both of the subsequent test periods. This was done to control for inter-observer bias.

Predicted values for each child's lung function measurements were calculated using published equations which account for the child's height at the time of testing, sex, and race<sup>14,15</sup>. Observed FEV<sub>1</sub> and FVC values were compared to the child's predicted values to obtain the percent of predicted at each measurement time. Acceptable data had to meet the test of reproducibility. The two highest FEV<sub>1</sub> values for each child were had to be within 0.1 liter of each other. Likewise, the two highest FVC values had to be within 0.1 liter of each other.

This report presents findings of the changes in FEV<sub>1</sub> over time. FEV<sub>1</sub> was considered to be the best spirometry variable for detecting airflow obstruction<sup>16,17</sup>.

**Survey.** In addition to spirometry, a questionnaire was developed using the ATS model<sup>18</sup> and mailed to the parents of children enrolled in the study. The survey sought information on the child's lung health, home exposure to woodstoves, tobacco smoke, cooking fuel and pet(s) along with other pertinent demographic, health, and socio-economic data.

**Analysis.** Data analysis examines the change (mean and standard average) lung function values over time. Analysis first compares the changes between the high and low outdoor exposure groups. The association of home woodstove usage and changes in mean lung function is examined by home use of a wood stove, independent of outdoor exposure area. Data are then analyzed combining home woodstove use and outdoor exposure area. The relationship between tobacco smoke and lung function is explored next. Finally, a multiple

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linear regression analysis is performed. This enables the interaction among the different variables to be examined.

**Ambient Monitoring.** Air monitoring for  $PM_{10}$  was conducted by the Department of Environmental Quality in both the high and low exposure areas. Peterson School, in the high exposure area, is the permanent site of an ambient air quality monitoring station which records continuous measurements on a year-round basis. This monitoring station reflected pollution levels for both schools in the high exposure area. A second station was set up at Conger School in the lower exposure area to measure  $PM_{10}$  levels during the study period.

Each station employed an integrating nephelometer which continuously monitored the smokiness of air by measuring the light scattering coefficient inside a chamber. Hourly levels were calculated by an internal computer. Due to limited availability of the equipment, ambient air monitoring in the low exposure area was only conducted between early November, 1989, and mid-March, 1990.

## Results

$PM_{10}$  air pollution levels in Klamath Falls were lower during the winter of 1989-90, than those recorded in previous years. (See Figure 1 for comparison). This was due in part to warmer than usual winter temperatures as well as an increased level of voluntary compliance with local efforts to reduce woodstove use during air inversion episodes. In addition to being less intense, the pattern of air inversions differed from previous years. The most severe and persistent inversions occurred during December instead of the period from late January through March--as in prior years.

Comparison of 24-hour average  $PM_{10}$  levels between high and low exposure areas is presented in Figure 3. Particulate levels measured in the high exposure area around Peterson School exceeded the NAAQS on 45 days during the 1989/90 heating season. Particulate levels were consistently lower in the area around Conger School (the low exposure area), exceeding the NAAQS only once during the study period.

A total of 464 elementary school children were originally enrolled in the study. Three completed sets of acceptable lung function measurements were obtained from 410 (88.4%) of the children. Data from the child health survey were received for 310 (75.6 percent) of these children. Children, for whom complete lung function data or survey information were lacking, did not differ significantly from the remainder of the study population in terms of age, sex and area of residence.

Table 1 presents the demographic characteristics of the children in the study for whom we had three complete sets of acceptable data. Forty-nine percent of the study population were males, and 51 percent were females. The overwhelming majority of the population was white. A small number of Hispanic, Native American, and African American students were also included in the study population. This pattern closely reflects the racial make-up of the three schools studied.

The average age of the children was 10 years, with a range from 7 to 14 years of age. Peterson Elementary School accounted for 44 percent of the study population, while Stearns School accounted for approximately 38 percent, and Conger School 18 percent. The level of participation in the study was 69% of eligible children from Peterson School, 60% of eligible children from Stearns School, and 66 percent of eligible children from Conger School. Children from Peterson and Stearns Schools live in the high exposure area of the study ( $n = 335$ ). Children from Conger School live in the low exposure area ( $n = 75$ ).

Table 2 presents a comparison for selected demographic and related characteristics between high and

low exposure areas. The average length of residence in the community was similar for children living in both the high and low exposure areas, based on the responses from parents to the child health questionnaire. Children in the high exposure area (Peterson and Stearns Schools) had a mean length of residence of 5.0 years. Children in the low exposure area (Conger School) lived in the area for an average of 5.4 years. The difference was not statistically significant.

The average reported level of parental income for the high exposure area was \$29,000, and \$32,000 for the low exposure area. This difference was not significant.

Mother's level of education was the same for both exposure areas, 13 years. However, father's level of education differed between the two exposure areas. Fathers in the high exposure area had completed an average of 12 years of school, while fathers in the low exposure area completed an average of 14 years of school. This difference was significant ( $p < .001$ ).

Reported woodstove use was similar for both exposure groups. In the high exposure area, 72.5% of the children lived in homes that used a woodstove for part or all of their heating needs. Among children in the low exposure area, 70.7% lived in homes that utilized woodstove heat.

Tobacco smoke exposure was known for 276 of the children. In the high exposure group, 64% of the children were reported to have some exposure to tobacco smoke. This compares to only 46% of the children in the low exposure group. This difference was significant at the  $p = .02$  level.

Asthma status was determined for each child through the child health survey. Approximately 10 percent of the children had been diagnosed by a physician as being asthmatic. Another 19 percent of the children had two or more symptoms compatible with undiagnosed asthma. The distribution of asthmatics was similar between high and low exposure areas.

Change in mean (average) PFT as measured by  $FEV_{1.0}$  was calculated for each exposure area (see Figure 4 and Table 3). Children in the high exposure area showed a decrease in the mean  $FEV_{1.0}$  from baseline (Time-1) to winter (Time-2). The average values declined 2.3% during this interval ( $p = .002$ ). The mean  $FEV_{1.0}$  declined an additional 2.2% from the winter (Time-2) to Spring (Time-3) measurements ( $p < .001$ ).

Children in the lower exposure area showed essentially no change in mean  $FEV_{1.0}$  between Time-1 and Time-2 (see Figure 4 and Table 3). There was a slight decline (0.8%) in mean  $FEV_{1.0}$  from Time-2 to Time-3.

Figure 5 presents mean  $FEV_{1.0}$  levels by woodstove exposure for the entire population. Children in homes where woodstove heat was used experienced a decline in  $FEV_{1.0}$  of 2.7% between Time-1 and Time-2 (see Table 4), while those children in homes without woodstove heat experienced no change in lung function during the same time frame. Both exposure groups showed declines in mean  $FEV_{1.0}$  values between Time-2 and Time-3 (-1.7% for those exposed to a woodstove in the home and -3.0% for those not exposed).

The impact of woodstove use was examined by exposure area (Figure 6). Children in the high exposure area who live in homes with wood heat had significant declines in  $FEV_{1.0}$  from Time-1 to Time-2, and again from Time-2 to Time-3 (3.3%  $p < .001$  and 1.5%  $p = .05$ , respectively (see Table 5)).

Children living in the high exposure area who did not have woodstove heat in their homes had essentially no change in lung function (0.8%) from Time-1 to Time-2. They did, however, exhibit a significant decline between Time-2 and Time-3 (4.2%  $p < .001$ ).

Children in the lower outdoor exposure area, who live in homes heated by woodstoves showed no change (0.2% decline) in mean  $FEV_{10}$  between Time-1 and Time-2. These children did, however, show a decline in lung function of 2.5 % from Time-2 to Time-3 ( $p = .004$ ).

Children in the lower exposure area who live in a home with no woodstove showed a statistically insignificant increase in lung function of 2.7%, from Time-1 to Time-2. This pattern of increase continued from Time 2-to Time-3 (1.1% increase).

Figure 7 presents the mean  $FEV_{10}$  over time, by tobacco exposure, for all children for whom this was known. Children with no reported exposure to tobacco smoke baseline levels markedly higher than children who were exposed to tobacco smoke (94.8%, 92.2%, respectively). These differences, however, were not statistically significant (see Table 6). Mean lung function declined 2.5% ( $p = .02$ ) between Time-1 and Time-2 for children with no tobacco exposure, while children who were exposed to tobacco smoke had declines of 0.8% (not significant). Both groups experienced similar declines between Time-2 and Time-3 (-1.7% for the not exposed group and -2.2% for the exposed group). The numbers of subjects with information about smoking are too small to conduct analysis by either exposure area or woodstove use.

The major variables of interest were combined in a multiple linear regression analysis. Outdoor exposure area and home use of a woodstove were both significantly associated with declines in  $FEV_{10}$  between Time-1 and Time-2. Exposure to tobacco smoke, asthma status, parent's income, and parent's education were not statistically associated with changes in  $FEV_{10}$ .

#### Summary

Temperatures were warmer during the winter of 1989/90 than in previous years when  $PM_{10}$  levels had been measured. Pollution levels were also lower during this winter and they occurred in December which was earlier than in previous years. Monitoring stations demonstrated that ambient  $PM_{10}$  pollution levels were consistently higher in the high exposure area than in the low exposure area.

There were no differences between the two outdoor exposure groups in terms of age, race, parental income, length of residence in the community, or the use of woodstoves for heat. The two groups were statistically different in terms of father's education, exposure to tobacco smoke, and exposure to ambient levels of  $PM_{10}$  pollution.

Significant decreases  $FEV_{10}$  from baseline (Time-1) to winter (Time-2) were observed among children in the high exposure schools. Significant decreases in  $FEV_{10}$  were also observed between Time-2 and Time-3 (after the winter heating season) among children in the high exposure area.  $FEV_{10}$  also declined during this latter time period among children in the lower exposure area. Among the study population, asthma status was not associated with a decline in lung function.

Children in homes heated by woodstoves showed greater declines in  $FEV_{10}$  than children in homes that did not use woodstove heat. The association between home woodstove use and lung function was evident among children living in both high and low outdoor pollution exposure areas.

Lung function measures either remained low or declined further between Time-2 and Time-3. This was an unexpected finding, seen among virtually all of the children in the study population. It is possible that a greater amount of time is needed for lung function to return to normal (baseline) following approximately five months of exposure to elevated  $PM_{10}$  levels. It is also possible that some event or exposure, unexplained by the variables analyzed, was the cause of this decline.



## CONCLUSIONS

Analysis of the data indicates that there was a significant decrease in average pulmonary function measurements among children in the high exposure area during the winter months when outdoor  $PM_{10}$  levels were elevated. This finding is consistent with results from other studies published in the literature.<sup>12</sup>

Additionally, the results of this pilot study found indoor woodstove exposure during winter months to be significantly associated with declines in children's  $FEV_{1.0}$  levels. Indoor woodstove exposure may be an important determinant of children's lung function than exposure to outdoor  $PM_{10}$  air pollution. Further study is needed to test this hypothesis.

Children in this study, who were exposed to tobacco smoke at the time of the baseline spirometry measurements had markedly lower lung function measurements than children who were not exposed. Children not exposed to tobacco smoke had significant declines in lung function measurements during the period of increased ambient  $PM_{10}$  pollution levels. Their mean  $FEV_{1.0}$  levels dropped to those of the children who were exposed to tobacco smoke.

This pilot study was not designed to be a definitive evaluation of the health effects of woodstove smoke exposure among elementary school aged children in Klamath Falls. A short time frame for planning and insufficient funding were clear limitations in this project. For example, we were unable to conduct a double baseline prior to the heating season, nor were we able to test pulmonary function during the peak exposure time which occurred earlier in the winter than was expected.

Furthermore, the focus of this study was to examine changes in pulmonary function among elementary school children over a specified time period. This study did not consider all possible health effects which may be associated with outdoor or indoor wood smoke air pollution exposure. Nor are the findings necessarily generalizable to other age groups which may be susceptible to this type of pollution.

Nevertheless, several significant associations have been identified in this study. Additionally, important questions are raised by this study which could be addressed through further investigation and with the appropriate funding. These questions include:

- A. What indoor pollutants are the children exposed to during the winter heating season?
- B. How do the indoor pollutant levels compare with outdoor levels for homes using woodstove heat versus homes with other sources of heat, and how is this affected by weatherization status?
- C. Would children's lung function changes be even greater if we had the flexibility to conduct testing at the absolute peak period of  $PM_{10}$  pollution?
- D. What is occurring during spring which might further affect children's lung function (eg., cumulative effects of air pollution exposure, high pollen counts, continued short duration [4-6 hours] high  $PM_{10}$  pollution levels occurring at nights, reaction to ambient silica dust exposure, or outbreaks of respiratory illness)?

We hope to be able to address these questions in the future.

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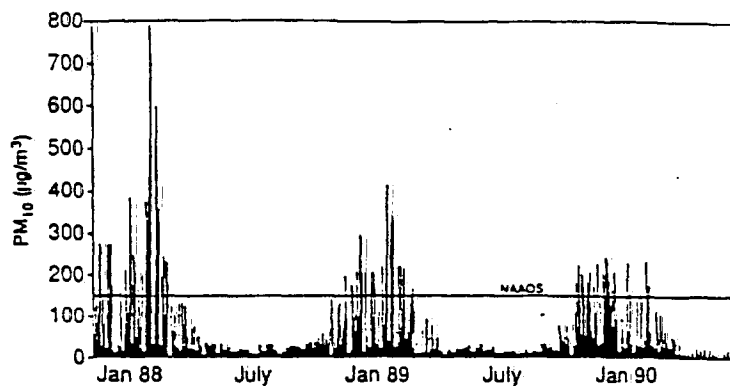


FIGURE 1 Klamath Falls  $PM_{10}$  levels.  
November 1987 to July 1990

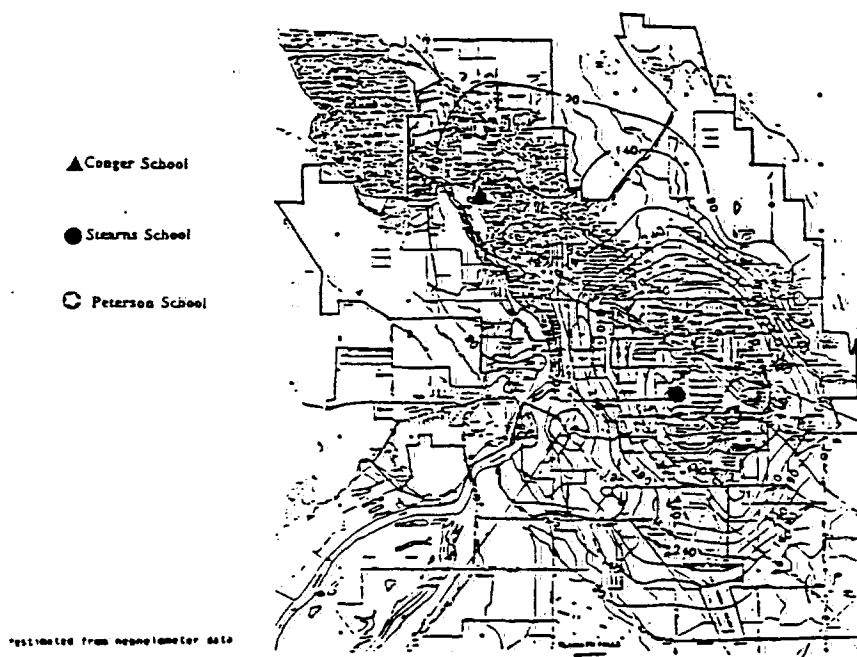


FIGURE 2 Klamath Falls nephelometer survey  
January 26, 1989, 9:00 p.m.  
( $\mu g/m^3$   $PM_{10}$ , 5 minutes averages)\*

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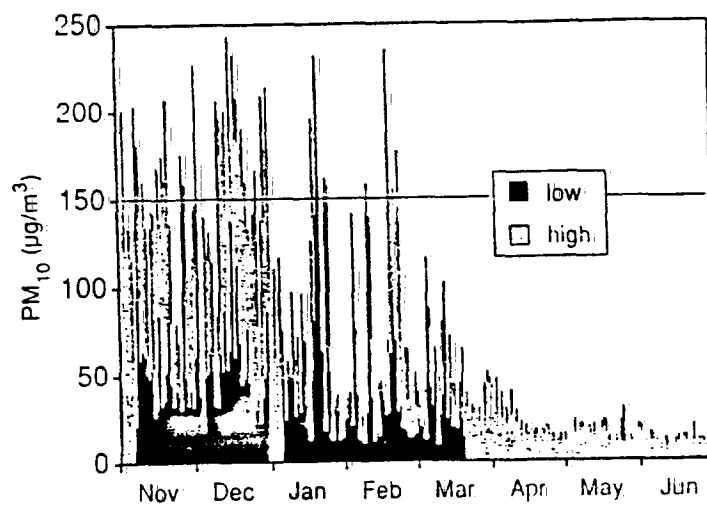


FIGURE 3 Klamath Falls PM<sub>10</sub> levels by exposure area.  
November 1989 - June 1990

NOTE TO EDITORS

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TABLE 1 Selected demographic variables  
for the study population, N = 410.

	Study Population	
	Number	Percent
SEX:		
male	201	49.0
female	209	51.0
RACE		
white	388	94.7
Hispanic	14	3.4
Native American	5	1.2
African American	3	0.7
AGE		
range	7 - 14 years	
median age	10 years	

TABLE 2 Selected demographic variables by exposure area

	High Exposure Area		Low Exposure Area		Level of Significance
	Number	(%)	Number	(%)	
AVERAGE LENGTH OF RESIDENCE in years	5.0		5.4		NS*
FAMILY INCOME median	\$29,000/year		\$32,000/year		NS*
PARENTAL EDUCATION					
Father (median)	12 years		14 years		p < .001
Mother (median)	13 years		13 years		NS*
HOME WOODSTOVE USE					
yes	166	(77.5)	41	(79.1)	NS*
no	63	(27.5)	10	(20.9)	NS*
ASTHMA STATUS					
physician diagnosed	24	(10.0)	7	(11.0)	NS*
history of symptoms	43	(18.3)	14	(20.3)	NS*
no asthma	168	(71.5)	40	(67.8)	NS*
TOBACCO EXPOSURE					
yes	140	(64.6)	25	(46.3)	.02
no	80	(36.4)	30	(53.6)	.02

\* Not Significant

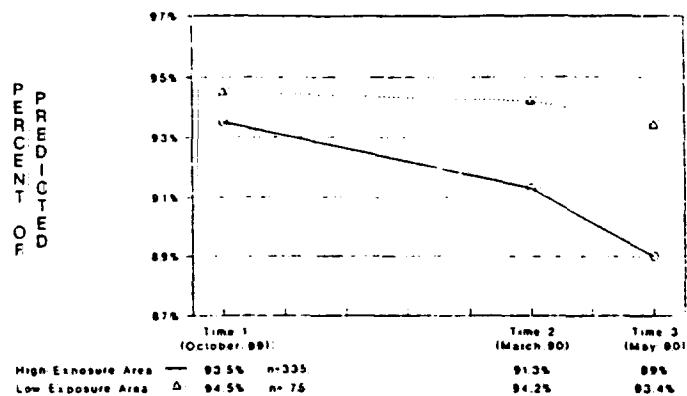


FIGURE 4 Change in mean FEV 1.0 for elementary school children by exposure area, N = 410.  
Klamath Falls, Oregon, 1990

TABLE 3 Change in mean lung function among elementary school children over the study period by exposure area, N = 410.  
Klamath Falls, Oregon, 1990

Exposure Area	Lung Function Measure	% of Change in Mean Value & Level of Significance			
		Baseline to Winter		Winter to Spring	
		%	P*	%	P*
High Exposure n = 335	FEV <sub>1.0</sub>	-2.3	.002	-2.2	<.001
	FEV/FVC	-1.1	<.001	-0.3	NS**
Low Exposure n = 75	FEV <sub>1.0</sub>	-0.3	NS**	-0.8	NS**
	FEV/FVC	-0.2	NS**	-0.7	.04

\*P = Level of Significance From Paired t-Test

NS\*\* = Not Significant at P = .05

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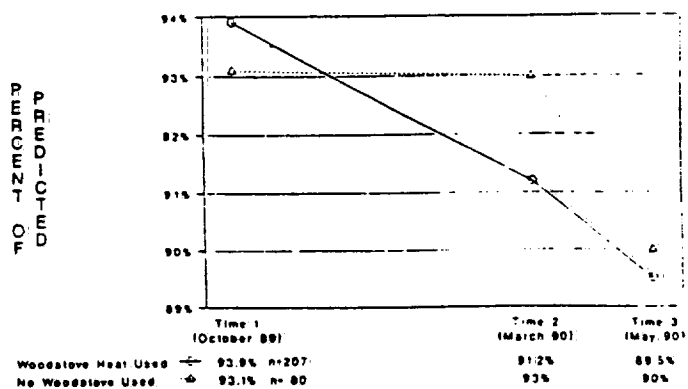


FIGURE 5 Change in mean FEV 1.0 for elementary school children, by home woodstove exposure, N = 287.  
Klamath Falls, Oregon, 1990

TABLE 4 Change in mean lung function among elementary school children over the study period by home woodstove use, N = 287.  
Klamath Falls, Oregon, 1990

Status of Woodstove Use	Lung Function Measure	% Change in Mean Lung Function			
		Baseline to Winter		Winter to Spring	Spring to Summer
		%	P	%	P
Home Woodstove Used N = 207	FEV <sub>1.0</sub>	-2.7	< .001	-1.1	.001
	FEV/FVC	-0.7	.001	-0.3	.001
No Woodstove Used N = 80	FEV <sub>1.0</sub>	-0.1	NS**	1.1	.001
	FEV/FVC	-1.3	.001	-0.3	.001

P = Level of Significance From Paired t-Test.  
NS\*\* = Not significant at P = .05.

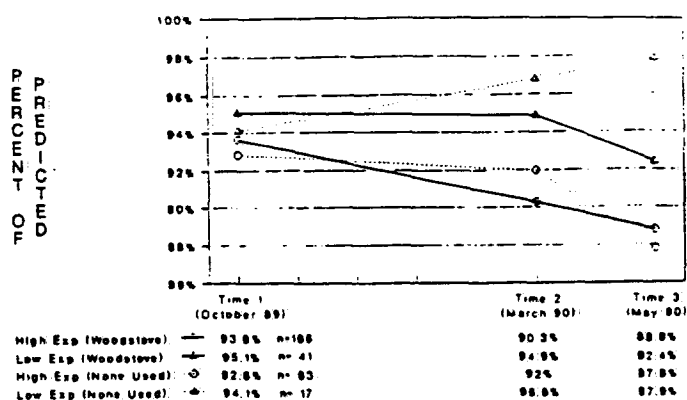


FIGURE 6 Change in mean FEV 1.0 for elementary school children, by exposure area and woodstove use, N = 287. Klamath Falls, Oregon, 1990

TABLE 5 Change in mean lung function among elementary school children over the study period by exposure area and by home woodstove use, N = 287. Klamath Falls, Oregon, 1990

Exposure Area	Lung Function Measure	Woodstove Used in Home				No Woodstove			
		Percent Change in Mean Value		Percent Change in Mean Value		Percent Change in Mean Value		Percent Change in Mean Value	
		Baseline to Winter	Winter to Spring	Baseline to Winter	Winter to Spring	Baseline to Winter	Winter to Spring	Baseline to Winter	Winter to Spring
High Exposure n = 229	FEV <sub>1.0</sub>	-3.3	< .001	-1.5	.05	-0.8	NS <sup>***</sup>	-4.2	< .001
	FEV/FVC	-0.7	NS <sup>***</sup>	+0.3	NS <sup>***</sup>	-1.4	.007	0.0	NS <sup>***</sup>
Low Exposure n = 58	FEV <sub>1.0</sub>	-0.2	NS <sup>***</sup>	-2.5	.004	+2.7	NS <sup>***</sup>	+1.1	NS <sup>***</sup>
	FEV/FVC	-0.3	NS <sup>***</sup>	-1.1	.04	-0.7	NS <sup>***</sup>	+0.3	NS <sup>***</sup>

\* = Level of Significance from Paired t-test  
 \*\* = Not Significant at P = .05



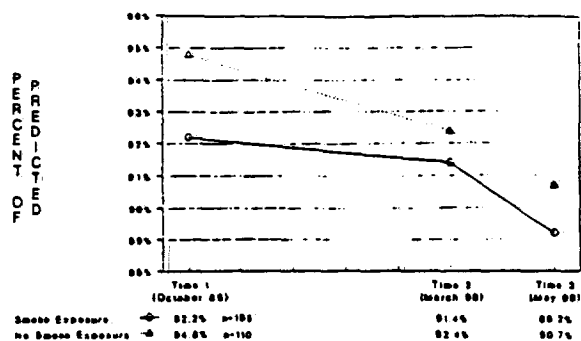


FIGURE 7 Change in mean FEV 1.0 for elementary school children, by tobacco smoke exposure, N = 276. Klamath Falls, Oregon, 1990


TABLE 6 Change in mean lung function among elementary school children over the study period by exposure to tobacco smoke, N = 276. Klamath Falls, Oregon, 1990

Exposure	Lung Function Measure	% of Change in Mean Value & Level of Significance			
		Baseline to Winter		Winter to Spring	
		%	P*	%	P*
Exposure to Tobacco Smoke N = 166	FEV <sub>1.0</sub>	-0.8	NS**	-2.2	.009
	FEV/FVC	-0.9	.023	-0.1	NS**
No Exposure N = 110	FEV <sub>1.0</sub>	-2.5	.02	-1.7	.03
	FEV/FVC	-0.8	NS**	0.0	NS**

\* = Level of Significance From Paired t-Test  
 \*\* = Not Significant at P = .05

37

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Lipsett, M., Ostro, B.D., Lipsett, M.J., Wiener, M.B., Selner, J.C., "Human Health and Environmental Effects. Session 136. Woodsmoke Exposure and Human Health Impacts: Effects of Exposures to Indoor Combustion Sources on Asthmatic Symptoms," Proc Annu Meet Exhib Air Waste Manage Assoc 15A(84): 1-16, 1991.

The authors presented preliminary results of an analysis of relationships between indoor and selected outdoor exposures and respiratory symptoms in a population of adult asthmatics residing in Denver, Colorado during the winter of 1987-1988. Outdoor exposures were measured daily. Estimates of indoor exposures were taken from daily diaries that the subjects filled out. The diaries also contained information on symptoms, medication use, utilization of medical services and other variables. The authors reported that "episodes of severe cough are strongly associated with the use of a fireplace or woodstove in men and women, suggesting an irritant effect of woodsmoke." The authors reported that gas stove usage was "an important factor" for women, while occupational exposure and domestic ETS were for men. The authors concluded that "this investigation documents a strong daily relationship between exposure to cigarette smoke and increased probabilities of clinically significant symptoms in free-living asthmatic adults."

91-136.6

**Effects of Exposures to Indoor Combustion  
Sources on Asthmatic Symptoms**

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## INTRODUCTION

Asthma is a chronic respiratory condition characterized by airway inflammation and intermittent episodes of bronchospasm that can be provoked by a variety of stimuli, including air pollution. Although there have been numerous controlled exposure investigations of the pulmonary effects of specific air pollutants on asthmatics<sup>1-5</sup>, relatively few epidemiologic studies have examined relationships between asthmatic status and exposure to both indoor and outdoor sources of air pollution.<sup>6-8</sup> While indoor concentrations of some pollutants (e.g., ozone) may reflect outdoor levels,<sup>9</sup> others are strongly influenced by the presence of combustion sources, including gas stoves, fireplaces and woodstoves, and cigarette smoking.<sup>10</sup> Indoor combustion produces a complex mixture of chemicals, many of which are respiratory irritants that may affect people with asthma, including nitrogen dioxide, aldehydes, acids and particulate matter.<sup>3,4,10-15</sup> In this paper we report preliminary results of an analysis of relationships between indoor (and selected outdoor) exposures and respiratory symptoms in a population of adult asthmatics residing in the Denver, Colorado metropolitan area during the winter of 1987 to 1988.

## DATA AND METHODS

### Study Population

Study participants were recruited from patients attending the clinic of one co-author (J.S.). Diagnosis of asthma was made in each case by history and signs of airway obstruction on physical examination, confirmed by spirometric demonstration of obstruction reversible with a  $\beta$ -agonist bronchodilator ( $> 15\%$  change in  $FEV_1$ ). Asthmatic patients were identified by clinic staff and were recruited for participation either during an office visit or by telephone and postcard contact. Denver residents between ages 18 and 70 were eligible to participate in the study if they had asthma currently managed with medication. Individuals with any other chronic medical condition that would restrict their activity were excluded.

This panel of asthmatics was asked to record, on a daily basis for several months, information about symptoms, medication use, utilization of medical services, indoor exposures, and other variables described below. A panel study has several advantages over other investigative designs. First, it provides a large number of observations, increasing the degrees of freedom and the stability of any estimates. Second, problems of confounding, omitted variables, and exposure assessment, while always present, are substantially reduced since individuals serve as their own controls over time. Thus, the impact of factors that vary daily, such as air pollution, can be isolated while other factors are held constant. Third, the consideration of a given sample in one metropolitan location over time eliminates the potential for any intercity confounding.

#### Health Measurements and Covariates

After giving informed consent, participants were required to fill out an intake questionnaire providing background data on demographics (age, sex, race, level of education, employment status, residential history), asthma severity and characteristic triggers and symptoms, medical history including medication use, smoking history, and previous environmental exposures. A diary instrument was designed to provide daily information on asthma symptoms, including the presence and severity on a scale of 0 to 4 (0=none, 1=mild, 2=moderate, 3=severe, 4=incapacitating) of cough, wheeze, shortness of breath, chest tightness, and sputum production, as well as physician and emergency room visits. In addition, information was obtained on the frequency of medication use, time spent outdoors, exercise intensity and location (i.e., indoors or outside), and potential indoor exposure to sources of respiratory irritants including gas stoves, fireplaces and woodstoves, environmental tobacco smoke, and occupational exposures. Participants were told that this was an investigation of environmental factors affecting asthma, but not that the principal variables of interest were air pollutants.

There were 330 intake questionnaires distributed (93 during office visits and 237 by mail) from November 15 to December 16, 1987. Of the initial group recruited, 256 returned the intake questionnaires. Study subjects were contacted by clinic staff intermittently throughout the study period (December 1987 through February 1988) to enhance compliance and continued participation. Ultimately, 207 patients submitted daily diaries, of which 182 contained complete information on indoor exposures. Table 1 displays the demographic characteristics and asthma severity for the latter group, who were predominantly white, female, employed and well educated, with an average age of approximately 46. The mean subjective asthma rating of moderate to severe is supported by the relatively large proportion of individuals taking daily oral theophylline and steroid preparations.

#### Exposure Measurement

Both outdoor and indoor air pollutants were considered as exposure measures. The ambient air pollutants available for the analysis were daily measures of sulfates, nitrates, PM<sub>2.5</sub>, nitric acid, hydrogen ion ( $H^+$  -- an index of airborne acidity), and sulfur dioxide. Previous analysis of the data<sup>16</sup> indicated that, of the outdoor pollutants,  $H^+$  was most strongly and consistently associated with respiratory symptoms and overall asthma status (though daily sulfate was also associated with one symptom -- shortness of breath). Therefore,  $H^+$  was the sole outdoor pollutant used in this examination of the potential health effects of indoor air.

Daily measurements (9:00 a.m. to 4:00 p.m.) of  $H^+$  were made at two monitors: one in downtown Denver, located about 2 miles from the clinic, and the other in the suburb of Arvada, located about 7 miles to the northwest. Because of problems in sample processing, the  $H^+$  data were available only for half of the study period. Therefore, missing values

were predicted using regression results with concurrent sulfate as the explanatory variable. With these substitutions, the daytime mean of  $H^+$  was 8.15 nanoequivalents (neq)/m<sup>3</sup> or approximately 0.4  $\mu\text{g}/\text{m}^3$  measured as sulfuric acid, with the highest daily average of 44 neq/m<sup>3</sup>. These levels are typical of urban areas.<sup>17</sup> Analysis of the two monitors recording  $H^+$  indicated that the concentrations of airborne acidity were fairly evenly distributed; the daily between-site correlation of the readings was 0.88. Thus, the one downtown monitor was used to represent daily levels of  $H^+$ . Ozone concentrations, which frequently are highly correlated with sulfates and acids in the summer, were essentially at background levels through the winter in Denver (i.e., the maximum one-hour concentration was 0.042 ppm) and were not correlated with  $H^+$  concentrations.

Data on indoor exposures were based on binary responses in the daily diary. No measurements of indoor concentrations were undertaken. The questions in the diary were:

Were you exposed to irritating smoke, dust or fumes today at work?  
 Were you exposed to cigarette smoke at home today?  
 Did you use a gas stove today?  
 Did you use a fireplace or wood stove today?

Table 2 provides descriptive statistics for the indoor and outdoor pollutants, meteorologic and health variables. The correlations between indoor exposures and outdoor pollution ( $H^+$ ) are low (Table 3). All data from questionnaires, daily diaries, air quality and meteorologic monitoring were coded and edited in a SAS format for analysis.

#### Statistical Methods

In this analysis, three different health outcomes were used as dependent variables in logistic regressions: the probability of a respondent reporting on a given day a moderate (or worse) cough, moderate (or worse) shortness of breath, and severe cough. The latter measure was included in order to examine more closely the relationship of indoor exposures to serious symptoms. As a daily average, 17.2 percent (range: 8.7 to 33 percent) reported moderate or worse cough, and 17.8 (range: 9.1 to 28 percent) reported moderate or worse shortness of breath, and 3.8 percent reported severe cough (range: 0 to 10.3%) (Table 2).

We estimated effects on each health outcome using logistic regression models. Based on earlier analysis,<sup>16</sup> the other variables included in the regressions were outdoor air pollution (i.e.,  $H^+$ ), the number of the day of the survey (to correct for secular trends in reporting) and whether the individual reported a symptom on the previous day. Neither temperature nor humidity was related to health status and both were excluded from subsequent analysis. The impact of indoor air pollution was estimated by considering each source separately in a regression equation. The models were applied to men and women separately and combined.

A different model was used to examine the impact of fireplaces and woodstoves. Exposure to emissions from this indoor source may be determined in part by the dependent variable in the regression; that is, the occurrence of a moderate or worse respiratory symptom may influence the decision to use a fireplace or woodstove. This potential simultaneity violates a fundamental assumption underlying regression analysis that the error term be independent of any of the explanatory variables. In order to address this potential problem, we used a simultaneous system of equations.<sup>18</sup> In this system, we first developed a regression equation to predict the use of a fireplace or woodstove. This predicted variable was then independent of the error term and, when substituted for the indicator variable (fireplace or woodstove use), generated an unbiased estimate.

#### RESULTS

Table 4 displays the results of the logistic regressions for the outcome of moderate or worse cough. The estimated coefficients for outdoor air pollution, measured as hydrogen ion, are presented with the four indoor air pollution sources, each considered separately in a regression. For the total sample, both the air pollution effect and all four indoor sources were associated with the probability of reporting a moderate or worse cough. Other significant influences on this dependent variable were the day of the survey and the occurrence of cough on the preceding day. For men, all four indoor sources were statistically significant, but outdoor  $H^+$  was not. For women, outdoor air pollution was statistically associated with cough, while among the indoor sources only gas stove use was significant.

Table 5 displays a similar set of coefficients for the outcome of moderate or worse shortness of breath. Again, for the sample as a whole, both the outdoor air pollutant and all four indoor sources were statistically significant. In general, this result also held for both men and women. For severe cough in the entire sample as a whole, only the indoor sources were statistically significant (Table 6). For men, daily woodstove or fireplace use, exposure to occupational irritants and to residential tobacco smoke were all associated with the probability of severe cough. For women, gas stove and fireplace or woodstove use were significant.

Table 7 summarizes the increases in probability of moderate or worse cough attributable to indoor pollutant exposures. For example, use of a gas stove on a given day would correspond to 10.1% increase in the probability of moderate or severe cough in this study population.

#### DISCUSSION

The results of this preliminary analysis suggest that both outdoor air pollution and indoor sources of combustion play important roles in the exacerbation of cough and shortness of breath in a population of adult asthmatics. In a previous paper,<sup>16</sup> we showed that, among the measured outdoor air pollutants, ambient airborne acidity was most consistently related to the occurrence of these symptoms. This analysis focuses on the impact of several indoor sources: gas stoves.



environmental tobacco smoke, fireplaces or woodstoves, and occupational exposures. For moderate or severe cough, men appear to be more susceptible to the effects of the indoor versus the outdoor pollutants, while the opposite is true for women. Further analysis is required to determine whether this disparity in gender-specific responses reflects differences in exposure time or intensity, asthma severity, or in the entire pattern of activities and joint exposures. It is possible, however, that the variation in the results for men and women may be attributable to the different sample sizes.

Shortness of breath in both sexes appears to be associated with ambient  $H^+$  concentration and with all the indoor exposures. Episodes of severe cough are strongly associated with the use of a fireplace or woodstove in men and women, suggesting an irritant effect of woodsmoke. As for the relationship of the other indoor exposures to this outcome, gas stove use was an important factor for women, while occupational exposure and domestic environmental tobacco smoke were for men. It is reasonable to postulate that the myriad respiratory irritants produced by domestic combustion bear a direct causal relationship to the symptoms reported in this study. There may also be indirect interactions among the pollutants, e.g., increased bronchial reactivity from exposure to  $NO_2$ <sup>3,4</sup> in gas stove emissions may lower the threshold of response to substances in woodsmoke and environmental tobacco smoke. Such potential interactions are the subject of ongoing research.

Though it is widely recognized that people spend most of their time indoors, relatively few epidemiologic investigations have attempted to analyze the relative contributions of indoor and outdoor air pollution to the respiratory status of asthmatics.<sup>6-8</sup> In these studies, asthmatic symptoms were found to vary by season, with different combinations of outdoor and indoor (specifically, gas stoves and passive smoking) exposures significant at different times of the year. The results reported here are consistent with these other investigations, and also include quantitative estimates of the magnitude of the effects of indoor sources. In addition, we have found that ambient  $H^+$  and use of a woodstove or fireplace significantly affect the probability of moderate or severe cough and shortness of breath. To our knowledge, this is the first empirical demonstration of this effect of woodsmoke on daily symptoms in adult asthmatics. Our findings are corroborated by other recent work indicating that ambient woodsmoke affects pulmonary function in asthmatic children<sup>19</sup> and that exposure to forest fire smoke is associated with increased emergency room visits for exacerbations of asthma.<sup>14</sup>

Previous studies have shown an effect of parental smoking on exacerbations of childhood asthma and, in a controlled setting, that some asthmatics are consistently sensitive to cigarette smoke.<sup>11,12</sup> This investigation documents a strong daily relationship between exposure to cigarette smoke and increased probabilities of clinically significant symptoms in free-living asthmatic adults. We have found a quantitatively similar relationship between gas stove usage and respiratory symptoms, which would not necessarily have been predicted from controlled studies of asthmatics exposed to low levels of  $NO_2$  in environmental chambers.<sup>3,4</sup> It is possible that the effects we observed

are a result of the relative severity of the clinical status of the study participants, or are driven by exposure to by-products of gas combustion other than  $\text{NO}_2$ , such as nitrous acid. At least one other series of studies has found an acute effect of gas stove usage on asthmatic pulmonary function, but the magnitude of the effect is difficult to assess.<sup>6,8</sup> With the caveat that these are preliminary results, the principal public health implication of our findings is that individuals with moderate to severe asthma should reduce to a minimum their exposure to residential sources of combustion, including fireplaces or woodstoves, gas stoves, and tobacco smoke.

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Table 1. Characteristics of Patient Population

Mean Age	45.6
% Male	34.0
Race (%)	
White	96.5
Black	1.5
Other	2.0
Education(%)	
College	62.0
High School	37.0
Less than High School	1.0
Employment status (%)	
Employed outside home	70.0
Homemaker	10.5
Retired	13.5
Other	6.0
Mean subjective asthma severity rating (0=none, 4=incapaciting)	1.7
% Daily Theophylline	58.0
% Daily oral steroids	18.9
% Current smokers	3.0

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Table 2. Descriptive Statistics of Pollutant, Meteorologic and Health Variables.

Variable	N (days)	Mean	Std. dev.	Min.	Max.
H <sup>+</sup> (neq/m <sup>3</sup> )	74	8.15	8.20	0.59	44.25
Minimum Temp (F)	105	17.71	11.97	-11.0	39.0
Moderate Cough (proportion/day)	74	.172	.049	.087	.33
Severe Cough	74	.038	.019	.000	.103
Moderate Shortness of Breath	74	.178	.034	.091	.280

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Table 3. Correlation Coefficients for Exposure to Indoor Sources, Ambient H<sup>+</sup> and Temperature.

	H <sup>+</sup>	Gas	Occup.	ETS	Fire
Gas	.00				
Occup.	.01	-.00			
ETS	.01	.04	.03		
Fire	.03	.09	-.02	.03	
Minimum Temp.	-.33	-.01	-.00	-.03	-.10

Note: H<sup>+</sup> = outdoor hydrogen ion concentration; Gas = gas stove; Occup. = occupational exposure; ETS = environmental tobacco smoke; Fire = fireplace or woodstove.

Table 4. Logistic Regressions Coefficients Relating Indoor and Outdoor Exposures to Moderate or Severe Cough.

<u>Exposure</u>	<u>All</u>	<u>Men Only</u>	<u>Women Only</u>
Log(H <sup>+</sup> )	.0892 <sup>a</sup>	.0035	.1278 <sup>a</sup>
Gas Stove	.7314 <sup>a</sup>	.8793 <sup>a</sup>	.6289 <sup>a</sup>
Log (H <sup>+</sup> )	.0699 <sup>b</sup>	-.0275	.1109 <sup>a</sup>
Woodstove or Fireplace	1.0571 <sup>a</sup>	3.3770 <sup>a</sup>	.6315
Log (H <sup>+</sup> )	.0873 <sup>a</sup>	.0097	.1247 <sup>a</sup>
Passive Smoke	.1943 <sup>b</sup>	.4774 <sup>a</sup>	.0336
Log (H <sup>+</sup> )	.0784 <sup>a</sup>	.0047	.1132 <sup>a</sup>
Occupational	.1342 <sup>c</sup>	.6272 <sup>a</sup>	-.1371

a =  $p < .01$ ; b =  $p < .05$ ; c =  $p < .10$

Table 5. Logistic Regression Coefficients Relating Indoor and Outdoor Exposures to Moderate or Severe Shortness of Breath.

<u>Exposure</u>	<u>All</u>	<u>Men Only</u>	<u>Women Only</u>
Log (H <sup>+</sup> )	.0967 <sup>a</sup>	.1018 <sup>b</sup>	.0962 <sup>a</sup>
Gas Stove	.6362 <sup>a</sup>	.4343 <sup>a</sup>	.7836 <sup>a</sup>
Log (H <sup>+</sup> )	.0734 <sup>a</sup>	.0613	.0788 <sup>b</sup>
Woodstove or Fireplace	2.4293 <sup>a</sup>	4.6984 <sup>a</sup>	1.0416 <sup>a</sup>
Log (H <sup>+</sup> )	.0957 <sup>a</sup>	.1110 <sup>b</sup>	.0936 <sup>a</sup>
Passive Smoke	.6145 <sup>a</sup>	1.1365 <sup>a</sup>	.2082 <sup>c</sup>
Log (H <sup>+</sup> )	.0892 <sup>a</sup>	.1004 <sup>b</sup>	.0864 <sup>a</sup>
Occupational	.3185 <sup>a</sup>	.7549 <sup>a</sup>	.0486 <sup>a</sup>

a =  $p < .01$ ; b =  $p < .05$ ; c =  $p < .10$



Table 6. Logistic Regression Coefficients Relating Indoor and Outdoor Exposures to Severe Cough.

<u>Exposure</u>	<u>All</u>	<u>Men Only</u>	<u>Women Only</u>
Log (H <sup>+</sup> )	.0278	.0069	.0343
Gas Stove	.7732 <sup>a</sup>	.3805	1.0607 <sup>a</sup>
Log (H <sup>+</sup> )	.0236	-.0308	.0333
Woodstove or Fireplace	1.7571 <sup>b</sup>	3.8546 <sup>a</sup>	1.8750 <sup>a</sup>
Log (H <sup>+</sup> )	.0264	.0186	.0327
Passive Smoke	.4363 <sup>a</sup>	1.0572 <sup>a</sup>	-.0415
Log (H <sup>+</sup> )	.0251	.0037	.0341
Occupational	.5233 <sup>a</sup>	1.2964 <sup>a</sup>	.0910

a =  $p < .01$ ; b =  $p < .05$ ; c =  $p < .10$

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Table 7. Estimated Magnitude of Effect of Indoor Sources on Moderate or Severe Cough.

Effect of Daily Exposure From:	Estimated Increase in Symptom Probability		
	All	Men	Women
Gas Stove	.104	.125	.090
Woodstove or Fireplace	.151	.481	NS
Passive Smoke	.028	.068	NS
Occupation	.019	.089	NS

NS = Estimated effect not significantly different from zero.

#### NOTE TO EDITORS

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38

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Behera, D., and Jindal, S.K., "Respiratory Symptoms in Indian Women Using Domestic Cooking Fuels," Chest 100: 385-388, 1991.

The authors studied "the effect of domestic cooking fuels producing various respiratory symptoms" in 3,701 women. The authors reported that "exposure to domestic cooking fuels produced a significant amount of respiratory morbidity" and that "use of smokeless devices and provision of adequate ventilation might be helpful to prevent some of these effects." Reportedly, the data suggested that smoking women exposed to such cooking fuels "experience respiratory symptoms more often than nonsmokers."

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# Respiratory Symptoms in Indian Women Using Domestic Cooking Fuels\*

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Surinder Kumar Jindal, M.D., F.C.C.P.

The effect of domestic cooking fuels producing various respiratory symptoms was studied in 3,701 women. Of these, 3,608 were nonsmoking women who used four different types of cooking fuels: biomass, LPG, kerosene, and mixed fuels. The overall respiratory symptoms were observed in 13 percent of patients. Mixed fuel users experienced more respiratory symptoms (16.7 percent), followed by biomass (12.6 percent), stove (11.4 percent), and LPG (9.9 percent). Chronic bronchitis in chulla users was significantly higher than that in kerosene and LPG

users ( $p < 0.05$ ). Dyspnea and postnasal drip were significantly higher in the women using mixed fuels. Smoking women who are also exposed to cooking fuels experienced respiratory symptoms more often than nonsmokers (33.3 percent vs 13 percent). (Chest 1991; 100:355-359)

ANOVA = analysis of variance; COHb = carboxyhemoglobin; LPG = liquified petroleum gas; MRC = Medical Research Council

Domestic cooking is one of the important functions for the average Indian housewife. The number of hours spent in the kitchen for domestic work and cooking is variable depending on the burden of extra work. On an average, an Indian housewife spends about six hours in the kitchen daily for cooking food and other purposes and because of sociocultural reasons, she is exposed to the fuel at an early age of about 15 years. Therefore, during her lifetime, she is exposed for 30 to 40 years, equivalent to 60,000 hours. The location of the kitchen, the type of ventilation, and the type of fuel used play a significant role on health. In most urban areas, the kitchens are located within the main house and the ventilation is generally good. In rural houses, most of the cooking is carried out in an enclosed space with poor ventilation because of cultural reasons and seasonal variations.

The type of cooking device used also is significant as far as indoor air pollution is concerned. Commonly, four types of cooking devices are available throughout this country. These include (1) kerosene stove (wick type or pressure type); (2) coal-lighted "angithi"; (3) gas stove operated by liquified petroleum gas (LPG); and (4) "chulla" in which biomass fuels (dried dung, crop residues, and agricultural wastes) are used. The amount of indoor air pollution or morbidity and mortality produced by these fuels has been discussed by various authors.<sup>1-4</sup> Padmavati and Arora<sup>5</sup> had suggested that the development of chronic bronchitis and

cor pulmonale in nonsmoking rural women may be due to the exposure to the smoke during cooking. In a preliminary study, Malik<sup>6</sup> had reported chronic bronchitis contributed by indoor air pollution in nonsmoking women. In the present study, an attempt is made to find out various respiratory symptoms in women using different cooking fuels.

## MATERIAL AND METHODS

A house-to-house survey was carried out in five villages situated about 5 km south of the Chandigarh city in Northern India. The area is free of any industrial or general atmospheric pollution. The villagers live in mud-walled or semi-pucca type of houses. The common cooking devices include chulla using biomass fuel, gas stove using LPG, kerosene stove, or a combination of two or more of these. The eligible population for this study consisted of every woman engaged in household cooking. The defined population numbered 4,259.

Detailed respiratory symptoms were revealed in a standard questionnaire adapted from that of the British Medical Research Council (MRC), and chronic bronchitis was diagnosed from the presence of cough with expectoration for three months in a year for at least two consecutive years on the recommended criteria of MRC.<sup>10</sup> Other symptoms noted were cough (falling short of the definition for chronic bronchitis), dyspnea in the absence of any clinical cardiopulmonary disease or severe anemia and obesity, bronchial asthma diagnosed on the history of episodic cough with wheezing, presence of rhonchi, response to bronchodilators, and postnasal drip. Basic demographic data, smoking history, location of the kitchen, adequacy of ventilation, and the type of cooking fuel used were also noted. Exposure index was calculated as the average number of hours spent daily for cooking multiplied by the number of years of cooking. Height was measured with the subject standing and without shoes.

The survey team consisted of one social worker, one technician, and a medical physician. The same team surveyed the whole population and the questionnaire was administered and filled out by the social worker after carefully explaining each question to the individual. A detailed physical and clinical examination was done by the visiting physician. Spirometry was carried out by means of a portable electronic spirometer (Spiroscreen, Gould, Singapore).

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Table 1—Age, Height, and Exposure Index of the Subjects (Mean  $\pm$  SE)

Fuel	Age, yr	Height, cm	Exposure Index
Chulla			
Symptomatic n = 126	36.9 $\pm$ 1.1	153.5 $\pm$ 0.5	77.5 $\pm$ 4.8
Asymptomatic n = 674	29.0 $\pm$ 0.4	153.1 $\pm$ 0.2	56.1 $\pm$ 1.7
p value	<0.001	>0.05	<0.001
Stove			
Symptomatic n = 129	29.6 $\pm$ 0.6	152.3 $\pm$ 0.6	43.2 $\pm$ 3.1
Asymptomatic n = 1,000	27.1 $\pm$ 0.2	152.0 $\pm$ 0.2	35.3 $\pm$ 0.9
p value	<0.01	>0.05	<0.05
LPG			
Symptomatic n = 48	34.9 $\pm$ 1.8	153.1 $\pm$ 0.8	53.1 $\pm$ 5.8
Asymptomatic n = 437	31.5 $\pm$ 0.5	153.0 $\pm$ 0.3	48.1 $\pm$ 2.0
p value	>0.05	>0.05	>0.05
Mixed			
Symptomatic n = 166	33.8 $\pm$ 0.9	153.4 $\pm$ 0.4	52.4 $\pm$ 3.6
Asymptomatic n = 626	26.2 $\pm$ 0.4	152.2 $\pm$ 0.2	36.9 $\pm$ 1.2
p value	<0.001	>0.05	<0.001

after explaining and demonstrating the procedure to each individual. Three graphs were obtained in each patient and the best one was chosen as the representative value for the individual.

The survey team was first trained in the laboratory in the technique of interviewing and carrying out spirometry. Periodic checking was done to verify the accuracies of the survey by a senior consultant of the department.

Data were analyzed by means of statgraphics v 3.0 on a computer (IBM PC XT): Cross table  $\chi^2$  test and analysis of variance (ANOVA) was used for statistical analysis.

## RESULTS

A total of 3,716 women were studied that covered 67.3 percent of the total female population. The remaining 13 percent of the women could not be studied because either they did not consent to participation or they could not be contacted on repeated visits. After excluding those with history of smoking (n = 93, 2.5 percent) and other concomitant diseases (n = 17), a total of 3,608 nonsmoking women were analyzed for the presence of respiratory symptoms. There were mainly four types of cooking fuels used by these women: chulla (biomass fuel); stove (kerosene oil); liquified petroleum gas (LPG); and mixed fuels such as a combination of two or more.

Table 1 shows the distribution of age, height, and exposure index in the population studied. The symptomatic women had higher age (p < 0.05 to 0.001)

except the LPG users. Similarly, the symptomatic women had higher exposure index in all fuel groups (p < 0.05 to 0.001) except the LPG users. The height was similar in all the groups. Table 2 shows different types of respiratory symptoms encountered by different fuel users. Mixed cooking fuels produced respiratory symptoms in 16.7 percent of the women. About 13 percent of chulla users and 11 percent of stove users encountered various respiratory symptoms. The overall respiratory symptoms were 13 percent in all groups of women.  $\chi^2$  tests across all cooking device categories revealed statistically significant differences in the symptoms (p < 0.01) and then individual comparisons were made using the  $\chi^2$  test. Chronic bronchitis in chulla users was significantly higher than that of kerosene stove and mixed fuel users (p < 0.05). Mixed fuel users experienced dyspnea and postnasal drip more often than other fuel users (p < 0.05). The prevalence of respiratory symptoms was more with increased exposure index in all the four groups of fuel users (Table 3). Table 4 gives various symptoms in smoking women using different fuels. Lung function parameters are given in Table 5. It was observed that asymptomatic women had higher values (percent predicted) for most of the parameters compared with symptomatic women (p < 0.05 to 0.01) except in the LPG group and in the mixed fuel users where the predicted FVC and FEV<sub>1</sub> values were comparable. Chulla users had lowest values for all four parameters (both symptomatic and asymptomatic).

## DISCUSSION

It is well established that all types of cooking fuels produce respiratory irritants such as oxides of nitrogen, sulphur dioxide, and unburnt hydrocarbons (soot particles).<sup>12,13</sup> Soot particles that are generated more with fire wood cooking chulla are probably more hazardous in causing changes of chronic bronchitis as well as airways obstruction. Chronic bronchitis in nonsmoking women has been reported to vary between 0.44 percent and 4.96 percent by various investigators from this country.<sup>14-17</sup> Wig et al<sup>14</sup> from Delhi had reported quite low frequency of chronic bronchitis in the rural nonsmoking women (0.44 percent). However, Malik and Behera<sup>15</sup> have reported

Table 2—Comparison of Symptoms in Different Fuels (Nonsmokers)\*

Fuel	Number studied	Chronic bronchitis*	Cough	Dyspnea†	Bronchial Asthma	Postnasal Drip‡	Total§
Chulla	1,000	29 (2.9)	10 (1.0)	77 (7.7)	5 (0.5)	5 (0.5)	126 (12.6)
Stove	1,129	15 (1.3)	9 (0.8)	75 (6.6)	10 (0.9)	20 (1.8)	129 (11.4)
LPG	485	12 (2.5)	3 (0.6)	27 (5.6)	1 (0.2)	5 (1.0)	45 (9.9)
Mixed	994	12 (1.2)	6 (0.6)	121 (12.2)	6 (0.6)	21 (2.1)	166 (16.7)
Total	3,606	66 (1.9)	26 (0.8)	300 (5.3)	22 (0.6)	51 (1.4)	469 (13.0)

\*chulla vs stove and mixed p < 0.05, †mixed vs chulla and stove p < 0.05, ‡mixed vs chulla p < 0.05, §mixed vs LPG p < 0.05

Numbers in parentheses indicate percentage.

Table 3—Symptoms According to the Exposure Index\*

Exposure Index	Fuel							
	Chulla		Stove		LPG		Mixed	
	Symptom No.	Total No.	Symptom No.	Total No.	Symptom No.	Total No.	Symptom No.	Total No.
<20	21 (6.8)	309	37 (8.9)	417	9 (6.5)	319	41 (12.02)	340
21-30	12 (13.5)	89	21 (10.3)	204	8 (14.3)	56	22 (15.0)	147
31-40	10 (10.2)	98	19 (12.6)	151	6 (9.4)	64	24 (21.1)	114
41-50	11 (18.03)	61	11 (12.6)	87	4 (8.7)	46	15 (14.1)	107
>50	72 (16.2)	443	41 (15.2)	270	21 (11.7)	180	64 (22.4)	286

\*Numbers in parentheses indicate percentage.

Table 4—Respiratory Symptoms in Smoking Women Exposed to Cooking Fuel\*

	Number Studied	Chronic Bronchitis	Cough	Dyspnea	Postnasal Drib	Total
Chulla	19	3 (15.8)	—	3 (15.8)	—	6 (31.6)
Stove	24	—	1 (4.2)	2 (8.3)	3 (12.5)	6 (25)
LPG	1	—	—	—	—	—
Mixed	49	7 (14.3)	2 (4.1)	10 (20.4)	—	19 (38.8)
Total	93	10 (10.7)	3 (3.2)	15 (16.1)	3 (3.2)	31 (33.3)

\*Numbers in parentheses indicates percentage.

a higher prevalence rate up to 4.96 percent from Chandigarh. Charan,<sup>16</sup> in a large study from rural Punjab, reported chronic bronchitis in 53 (0.74 percent) of 7,132 subjects. These studies have not paid particular attention to the role of cooking fuels, although speculation was made about its role in the causation of chronic bronchitis. Thiruvengadam et al<sup>17</sup> from Madras (Southern India) have also reported the prevalence of chronic bronchitis to be 1.5 percent in female subjects. Similarly, a low prevalence of chronic bronchitis has been reported from Nigeria (0.24 percent),<sup>18</sup> Zimbabwe (2.8 percent),<sup>19</sup> Japan (3.1 percent),<sup>20</sup> and Uppsala (1.5 percent)<sup>21</sup> in nonsmoking

women. However, only one study from Nepal<sup>8</sup> has shown a high prevalence of chronic bronchitis in 12.57 percent cases of nonsmoking women and directly attributed to domestic smoke pollution, particularly biomass fuel. Our present study shows an overall prevalence of chronic bronchitis of 1.9 percent and when analyzed for different cooking devices, it was 2.9 percent for chulla users. Cough, as reported by some women, does not fit the definition of chronic bronchitis. Perhaps these are a subset of patients with chronic bronchitis, and if history is taken, they will be diagnosed as having chronic bronchitis. Then the overall incidence will rise to 2.7 percent, which is still

Table 5—Lung Function Data (Percentage Predicted) in the Subjects Studied (Mean  $\pm$  SE)\*

Fuel	FVC	FEV <sub>1</sub>	PEFR	MMF
Chulla				
Symptomatic n = 126	71.56 $\pm$ 1.51	83.21 $\pm$ 1.89	63.43 $\pm$ 1.86	91.85 $\pm$ 3.02
Asymptomatic n = 845	76.53 $\pm$ 0.39	88.82 $\pm$ 0.57	67.77 $\pm$ 0.80	99.55 $\pm$ 0.96
p value	<0.01	<0.01	<0.05	<0.05
Stove				
Symptomatic n = 129	77.50 $\pm$ 1.27	88.78 $\pm$ 1.43	68.64 $\pm$ 1.81	93.67 $\pm$ 2.80
Asymptomatic n = 977	80.14 $\pm$ 0.37	90.29 $\pm$ 0.42	69.87 $\pm$ 0.60	97.70 $\pm$ 1.11
p value	<0.05	>0.05	>0.05	>0.05
LPG				
Symptomatic n = 48	78.71 $\pm$ 1.75	92.14 $\pm$ 2.18	66.07 $\pm$ 3.49	96.65 $\pm$ 4.38
Asymptomatic n = 426	77.98 $\pm$ 0.65	91.20 $\pm$ 0.78	68.57 $\pm$ 1.03	101.14 $\pm$ 1.61
p value	>0.05	>0.05	>0.05	>0.05
Mixed				
Symptomatic n = 166	75.81 $\pm$ 1.17	87.63 $\pm$ 1.40	65.87 $\pm$ 1.62	94.06 $\pm$ 2.26
Asymptomatic n = 797	77.39 $\pm$ 0.44	88.99 $\pm$ 0.61	70.74 $\pm$ 0.70	100.22 $\pm$ 0.99
p value	>0.05	>0.05	<0.01	<0.05

\*PEFR = peak expiratory flow rate; MMF = mean maximum flow.

far less than that reported by Pandey<sup>8</sup> from Nepal, although it is similar to that reported from this country as well as from elsewhere. The discrepancy between the Nepal study and the present one is perhaps due to total absence of ventilation facilities in Nepal houses producing much more pollution than the Chandigarh villages.

LPG or kerosene stove cooking, specifically the former, which is considered traditionally to be safe fuel, also produces a significant amount of respiratory symptoms. Dyspnea was one of the major complaints in these symptomatic women. In the absence of cardiopulmonary disease, severe anemia, or obesity, this symptom is quite interesting. It is possible that an average woman mistakes fatigue as dyspnea. According to Burney et al.,<sup>22</sup> high levels of blood carboxy-hemoglobin (COHb) may also be responsible for dyspnea. Although we have not measured COHb in these women, in an earlier study we have shown that high levels of COHb are seen in subjects exposed to biomass fuel.<sup>23</sup> Whether this is enough to explain dyspnea is not very clear.

Bronchial asthma, as mentioned in some cases, is unlikely to be due to cooking fuels. However, if such a patient is exposed to domestic fuel producing smoke, the symptom will be aggravated.

In an earlier study<sup>24</sup> in 642 teachers from the city of Chandigarh (urban population), we had observed bronchial asthma in 3.2 percent of female subjects and dyspnea was reported in 4.9 percent of non-smoking women. However, in the present study, in rural female subjects the symptoms were observed in 0.6 percent and 5.3 percent of subjects, respectively. This low incidence of bronchial asthma may not reflect the true prevalence since many patients with cough and dyspnea might be suffering from this condition. Evaluation of the adequacy of ventilation in production of the symptoms was difficult since quantification was not possible. However, we believed that, although most of the houses had provision for ventilation in the kitchen, this was not adequate. Thus, exposure to domestic cooking fuels produced a significant amount of respiratory morbidity. Use of smokeless devices and provision of adequate ventilation might be helpful to prevent some of these effects. Moreover, smoking women exposed to cooking fuels experience respiratory symptoms more often than nonsmokers.

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**2023510461**

# Domestic Pollution and Respiratory Illness in a Himalayan Village

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Norboo T (SNM Hospital, Leh, Ladakh, India), Yahya M, Bruce NG, Heady JA and Ball KP. Domestic pollution and respiratory illness in a Himalayan village. *International Journal of Epidemiology*, 1991; 20: 749-757.

Summer and winter surveys of a village in Ladakh have been used to study respiratory illness and domestic pollution from fires in an arid high altitude region of northern India. The prevalence of chronic cough with chronic phlegm rose steeply with age, and was greater among women than men. The percentage of villagers with a forced expiratory volume in one second/forced vital capacity (FEV<sub>1</sub>/FVC) ratio of less than 65% also rose with age, to include 24% of men and 32% of women over 50 years in the summer survey. Lung function was significantly worse in those reporting chronic cough, independently of age and sex ( $p < 0.001$ ). Carbon monoxide (CO) measurements were used to assess domestic pollution from fires. Amongst the small minority of smokers (all men) CO in exhaled air was higher than in non-smoking men. In non-smoking men and the women, levels of exhaled CO were very significantly higher in winter than in summer, as were the levels of CO measured in the houses. There was a fall in FEV<sub>1</sub> (but not FVC) between summer and winter ( $p < 0.0001$ ), and an association was found between individual change from summer to winter in exhaled air CO and the individual change in FEV<sub>1</sub> ( $p < 0.01$ ). A significant negative association was found between the winter value of CO in exhaled air and FEV<sub>1</sub>/FVC ratio in women ( $p < 0.05$ ), although a similar association in men was non-significant. No significant associations were found between winter pollution levels and the presence of chronic symptoms. During winter, fires without chimneys gave higher levels of house pollution and individual CO in exhaled air than those with chimneys ( $p < 0.01$ ). It is concluded that domestic pollution is an important contributor to chronic respiratory illness in this community, and that an intervention study is now required to establish the benefits to health of an improved fire design.

The village of Chuchot Shamma lies at an altitude of 3000 metres (11 200 feet) beside the river Indus, and about 15 km from Leh, the capital of Ladakh. This region lies in the rain shadow of the main Himalayan range and experiences a very low level of precipitation. Although its physical isolation has prevented rapid change, the recent expansion of tourism has provided some impetus for western style development, principally in and around Leh. Despite this contemporary influence, the culture of Ladakh which is historically closely linked to that of Tibet is generally well preserved.

For some years, physicians working in the Sonam Norboo Memorial Hospital in Leh had been concerned by the number of people from Chuchot with chronic lung disease suggestive of chronic bronchitis. Pollution from domestic fires was suspected of being a cause. Heating and cooking in the home is provided by fires burning wood and dried yak dung, and many of these fires either have no chimney, or at best emit a lot of smoke and fumes into the living accommodation. During winter, when outdoor temperatures can fall to  $-30^{\circ}\text{C}$ , families spend long periods in poorly ventilated and heavily polluted rooms. A graphic historical description of the situation is given in an account of the travels of William Moorcroft through this region in the 18th century.<sup>1</sup>

... He was appalled at the acrid smoke from the yak dung fires which filled every Ladakhi living room in winter and he often insisted that the fire be put out, or lay on the floor to clear his streaming eyes, before he could treat some of his sick patients.

Evidence from other highland communities in Nepal<sup>2</sup> and Papua New Guinea,<sup>3,4</sup> have identified high

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levels of domestic pollution and chronic lung disease which is thought to be chronic bronchitis. Although an association between time spent exposed to pollution and respiratory illness has been demonstrated in Nepal,<sup>2,3</sup> there is little other direct evidence of a causal link between biomass smoke and chronic lung disease. A survey of Chuchot was therefore carried out in order to investigate the prevalence of respiratory illness, and to study the relationship between the level of domestic pollution and the observed pattern of illness.

#### METHODS

Chuchot Shamma is one of three contiguous villages lying beside the Indus near Leh, and the economic activity, culture and the types of stove and fuel used are typical of the area. The first survey of the village was conducted during August 1987, and an attempt was made to contact all inhabitants aged 20 years and above using the electoral register. A total of 208 women were examined, an overall response rate of 74%, and of 76% or more in all age groups except the 20-29-year-olds (65%). Some 156 men were examined, an overall response rate of 53%. This varied more by age; 80% in those 50 and older, but only 44% for ages 20-49 years.

A second survey carried out during the following December (1987) and January (1988) sought to re-examine all subjects who had been successfully contacted during the previous summer. The re-examination response rate was similar to the first study, 78% overall for women and 56% for men, with a similar age pattern. The poor response for the younger men occurred because many left the village very early in the day to go to work in Leh, and this means that the effective response for younger males examined in both studies is very low (about 20%). The sample was 61% Moslem (the majority Shia) and 39% Buddhist, which reflects the known religious constitution of the village population. About 40% of the men were government employees and also farmers, and most of the rest solely farmers. The majority of women described themselves as housewives, but they are also farmers.

#### Summer Survey

An interview was conducted by a local doctor (MY), with questions on occupation and religion, smoking, and the standard MRC questions on cough and phlegm.<sup>6</sup> The responses to the questions on cough were divided into 'no cough', 'infrequent cough' and 'chronic cough'. A subject had 'chronic cough' if either morning cough in winter, or daytime/night-time cough in winter (or both) were reported, and this pattern of coughing was reported on most days for as much as

three months each year. A subject had 'no cough' if all answers were negative, and 'infrequent cough' if there was either morning cough in winter, or daytime/night-time cough in winter (or both) but which did not occur on most days for as much as three months each year. Analogous definitions were used for 'no phlegm', 'infrequent phlegm' and 'chronic phlegm'. Subjects were asked whether they smoked manufactured cigarettes, bidis (local Indian cigarettes), a hookah pipe, and whether they used snuff or chewing tobacco. The interview was followed by measurement of forced expiratory volume in one second (FEV<sub>1</sub>) and forced vital capacity (FVC) made with a Micromedical Pocket turbine spirometer, an instrument which has been validated elsewhere<sup>7</sup> and used previously in epidemiological fieldwork.<sup>8</sup> The measurements were made in the houses, and the highest of three readings was taken for analysis.

Carbon monoxide (CO) levels were used as a measure of pollution caused by domestic fires, and for validation of reported smoking habits. Two types of measurement were made. First, CO in the exhaled air of each subject was recorded with a Bedfont EC50 analyser. This was calibrated to zero prior to each test, and all measurements were made in a room away from lit fires. Second, measurements of ambient kitchen CO levels were made with the same instrument in a number of houses at three locations; over the fire ('fire'), in the middle of the kitchen at floor level ('floor'), and in the same place but at chest height ('middle').

#### Winter Survey

This consisted of an interview also carried out by MY which covered current smoking habits, and determined whether any fires were alight in the house, and whether or not these had a chimney pipe. Measurements of FEV<sub>1</sub> and FVC were then made using a Micromedical Micro turbine spirometer (the original summer instrument was not available), but using the same protocol. Spirometry was carried out in the houses, where the mean temperature was 11.9°C (SE 0.17). This compares to 23.5°C (SE 0.19) for the houses in summer. Although there was a difference of 11.6°C in room temperature, since the turbine of the spirometer is mounted in a closed tube which is held against the mouth, there is unlikely to be any important difference between the summer and winter surveys in the temperature of air reaching the turbine. Carbon monoxide in exhaled air was measured with the same Bedfont instrument, with subjects outdoors, or if indoors, away from a room with (or near) a lit stove. This was done to avoid air from the heavily pol-

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luted rooms being inhaled, and then breathed out into the CO analyser. Ambient CO levels were also measured at the same three locations in the kitchens. Questions about cough and phlegm were not asked again in the winter survey.

#### Smoking

In the summer survey, 35 (22.7%) of the men, and none of the women reported smoking cigarettes. Of the 35 male smokers, only 7 (20%) were aged 40 years or over, and this means that 42% of those under 40 were smoking cigarettes. The use of other forms of smoking material and tobacco was minimal. Seventeen of the men examined in both the summer and winter surveys were classified as smoking cigarettes, and one was aged 40 years or over. For analyses involving CO in exhaled air as a measure of pollution, smokers have been presented separately or excluded. All other analyses have been carried out with and without the smoking men, but since the exclusion of smokers made little difference, the results are presented for all men.

#### Statistical Methods

Three aspects of respiratory health care considered for the purposes of examining the associations with domestic pollution: (a) symptoms of chronic cough and of chronic phlegm; (b) lung function measured in winter, and (c) the individual change in FEV<sub>1</sub> between summer and winter. The distributions of CO in exhaled air, and particularly in the houses, were quite markedly positively skewed. Accordingly, the p-values derived from comparisons of CO levels in the different groups in Tables 3 and 6 have been carried out on the log-transformed data. Untransformed means and standard errors are given in both Tables in order to facilitate comparison with levels of exposure to CO found in other studies.

## RESULTS

### The Prevalence of Chronic Cough and Phlegm

Table 1 shows that the prevalence of both chronic

TABLE 1 Prevalence by age of chronic cough and of chronic phlegm in Chuchot Shamma, Summer survey

Age (years)	% with chronic cough		% with chronic phlegm	
	Men	Women	Men	Women
20-24	0	26.3	7.1	13.1
25-29	0	28.5	13.4	14.3
30-39	16.7	27.0	16.7	18.7
40-49	22.2	34.3	11.5	22.9
50-59	33.3	66.7	30.0	62.5
60+	67.7	78.9	48.4	63.2

cough and chronic phlegm rose quite steeply with age in the men and women examined in the summer survey. The women reported a higher prevalence of chronic cough than men at all ages, while the sex difference in chronic phlegm became prominent only after age 40. About one-quarter of the women aged under 30 in this sample reported cough on most days for three months during the winter, while none of the men under 30 did so (chi-square test = 8.06; df = 1;  $p < 0.01$ ). Overall, 63% of the men with chronic cough, and the same percentage of women with chronic cough, also had chronic phlegm. The prevalence of chronic cough with chronic phlegm by age is shown in Figure 1. The percentage of both men and women with chronic cough who also reported chronic phlegm increased markedly with age; for men it rose from 0% at 20-29 to 71% at 50 and over, while for women it rose from 39% at 20-29 to 87% at 50 and over.

#### Lung Function (Summer) and Symptoms

The overall mean FEV<sub>1</sub>/FVC ratio was 76.0% in the men and 76.9% in females, and became progressively worse with increasing severity of cough (Table 2). Males aged 50 and over with chronic cough had a ratio of 66.8% compared to 76.6% for those in the same age group reporting no cough, while values for females were 67.8% and 76.2% respectively. The relationship between symptoms and lung function was examined by

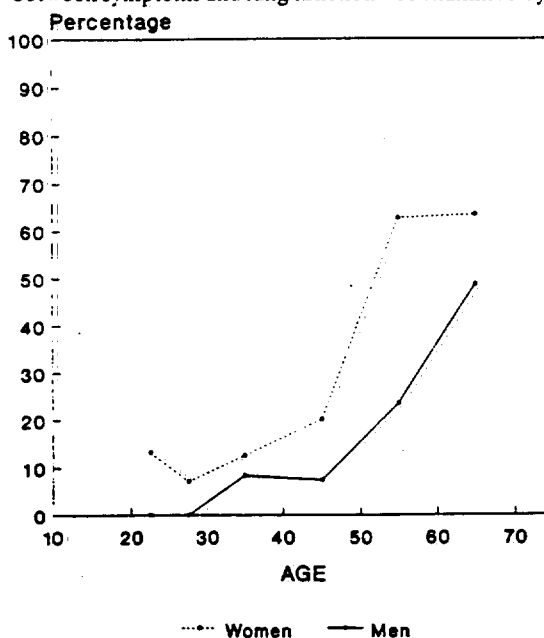


FIGURE 1 The prevalence of chronic cough with chronic phlegm (see text for definitions) by age among men and women in Chuchot (summer survey)

TABLE 2 Number of subjects examined in the summer survey, mean summer values of FEV<sub>1</sub>/FVC ratio (%) and standard errors for men and women by level of cough

Men		Level of cough			Total
Age group		None	Infrequent	Chronic	
20-34	n	33	6	3	42
	mean (S.E.)	82.3 (1.4)	82.8 (3.5)	79.8 (9.7)	82.2 (1.3)
35-49	n	22	8	9	39
	mean (S.E.)	75.7 (2.3)	76.4 (4.5)	73.1 (4.8)	75.2 (1.9)
50+	n	17	9	29	55
	mean (S.E.)	76.6 (2.4)	78.7 (4.4)	66.8 (2.2)	71.8 (1.6)
Total	n	72	23	41	136
	mean (S.E.)	78.9 (1.1)	79.0 (2.5)	69.1 (2.0)	76.0 (0.9)

Women		Level of cough			Total
Age group		None	Infrequent	Chronic	
20-34	n	58	8	26	92
	mean (S.E.)	81.6 (0.9)	80.7 (3.8)	77.2 (2.1)	80.3 (0.9)
35-49	n	32	7	19	58
	mean (S.E.)	77.0 (2.1)	74.8 (3.2)	74.9 (2.5)	76.0 (1.5)
50+	n	6	3	25	34
	mean (S.E.)	76.2 (4.5)	70.6 (2.1)	67.8 (2.1)	69.5 (1.8)
Total	n	96	18	70	184
	mean (S.E.)	79.7 (0.9)	76.7 (2.2)	73.2 (1.3)	76.9 (0.7)

multiple regression to take account of age and sex. FEV<sub>1</sub>/FVC ratio was, independently of age and sex, significantly lower in the group reporting chronic cough relative to those with no cough ( $p < 0.01$ ), but only slightly lower (and non-significantly) in those reporting infrequent cough. A similar pattern of deteriorating lung function with more severe symptoms was seen for chronic and infrequent phlegm ( $p < 0.05$ ).

The proportion of men and women with an FEV<sub>1</sub>/FVC ratio of less than 65% rose quite steeply with age, to include 24% of men and 32% of women aged over 50 years.

#### Pollution in Summer and Winter

Carbon monoxide levels in individual exhaled air were markedly higher in winter than in summer (Table 3a). The 17 men (examined in both surveys) who smoked cigarettes had CO levels in summer which were three times higher than non-smoking men, a highly significant difference. There was a smaller absolute increase in CO level between summer and winter among smokers as compared to non-smokers, but the higher level in smokers remained significantly above that for non-smokers in winter ( $p < 0.05$ ). The summer CO levels in women and non-smoking men were similar, but in winter were significantly higher in women ( $p < 0.05$ ). Ambient levels of CO at the three measure-

ment sites within the houses are shown in Table 3(b). These levels were not surprisingly highest close to the fires, and also showed marked increases from summer to winter at all three measurement locations. All  $p$ -values quoted for CO level comparisons relating to Tables 3(a) and (b) are of the log-transformed data.

#### Lung Function in Summer and Winter

Among the subjects examined in both surveys, the mean FEV<sub>1</sub> fell between summer and winter by 0.35 litres in men ( $p < 0.0001$ ), and by 0.17 litres in women ( $p < 0.0001$ ). FVC in men fell by only 0.04 litres and rose by 0.03 litres in women, and the  $p$ -values for these differences were well above 0.1.

Table 4 illustrates the summer and winter values of FEV<sub>1</sub>/FVC ratio by level of cough for the men and women who were examined in both surveys, and the change that occurred as a percentage of the summer value. The mean summer FEV<sub>1</sub>/FVC ratio for the subgroup of women who were seen in both surveys was 76.1%, and this compares well with the value of 76.9% for the whole summer sample of women (Table 2). In contrast, the summer FEV<sub>1</sub>/FVC ratio for men examined in both surveys was 71.9%, considerably lower than the summer value for men of 76.0% (Table 2), and this is probably the result of the poorer re-examination rate among the younger males.

The winter values of FEV<sub>1</sub>/FVC fell to 62.8% for

TABLE 3a Mean levels of carbon monoxide (CO), and standard errors in exhaled air of men (smokers, non-smokers and all men) and women, for those subjects with readings in both the summer and winter surveys

Individual exhaled air			Mean CO levels (ppm)			
Sex	Smoking	No.	Summer	Winter	Difference	p-value*
Men	Yes	17	16.5 (3.0)	20.4 (2.3)	3.9 (3.2)	NS
	No	64	5.5 (0.5)	13.9 (1.4)	8.4 (1.5)	<0.0001
	Both	81	7.8 (0.9)	15.3 (1.2)	7.5 (1.3)	<0.001
Women	No	157	5.7 (0.3)	17.3 (0.8)	11.5 (0.8)	<0.0001

men and 69.8% for women (Table 4), and there was a greater fall in the ratio for those reporting chronic cough compared to those with no cough ( $p = 0.05$ ). The winter values of FEV<sub>1</sub>/FVC ratio for those subjects reporting chronic cough were 53.2% for men and 65.5% for women. The fall in FEV<sub>1</sub>/FVC ratio for those reporting infrequent cough was only very slightly greater than those with no cough. There was some evidence of a similar interaction between the summer to winter change in FEV<sub>1</sub>/FVC ratio and the level of the symptom for phlegm, but this was weaker than for cough and did not reach significance at the 0.05 level.

#### Pollution and Respiratory Health

**Symptoms.** Logistic regression models with (i) presence or absence of chronic cough and (ii) presence or absence of chronic phlegm as outcomes were used to examine the relationships between these two chronic symptoms and individual exhaled air and room CO levels as recorded in winter. The models were adjusted for age, and for men restricted to non-smokers. None of the associations between any of the measures of CO and either chronic cough or chronic phlegm approached statistical significance.

**Lung function.** The relationships between winter lung function and winter CO levels were examined using linear regression, adjusted for age and height, and for men restricted to non-smokers. The associations between the FEV<sub>1</sub>/FVC ratio and the level of individual exhaled air CO were negative for both men and women; the regression coefficient for women, which

indicated a 0.19% fall in FEV<sub>1</sub>/FVC ratio for a 1 ppm increase in exhaled air CO concentration, was significant ( $p < 0.05$ ). The male regression coefficient of  $-0.17\%$  per 1 ppm increase in CO was not significant. The associations between FEV<sub>1</sub>/FVC ratio and the house measures of CO were also negative, but very weak. FEV<sub>1</sub> and FVC were both negatively (but non-significantly) associated with individual exhaled air and house CO levels in men. In women, with the exception of a non-significant negative coefficient for FEV<sub>1</sub> on individual CO, the associations between pollution levels and FEV<sub>1</sub> and FVC were positive but very weak.

**Individual summer to winter change in pollution and FEV<sub>1</sub>.** Smoking men were excluded from this analysis. A significant ( $p < 0.01$ ) positive association was found between the change in the level of exhaled air CO from summer to winter in each subject and the individual change in FEV<sub>1</sub> (Table 5). Although the magnitude of the fall in FEV<sub>1</sub> was greater among the men than women ( $p < 0.001$ ), the proportionate drop in FEV<sub>1</sub> across the range of increase in pollution was greater in the women (Table 5).

TABLE 4 Number of subjects, FEV<sub>1</sub>/FVC ratio % (and standard errors), in summer and winter for men and women who were examined in both surveys, by level of cough. The fall in FEV<sub>1</sub>/FVC ratio between summer and winter, expressed as a percentage of the summer value, is also shown

Level of cough	Group	No.	FEV <sub>1</sub> /FVC ratio		
			Summer	Winter	% fall
None	Men	31	75.1 (1.8)	67.7 (1.7)	9.9
	Women	56	78.5 (1.2)	73.1 (1.0)	6.9
	All	87	77.3 (1.0)	71.1 (0.9)	7.2
Infrequent	Men	12	77.1 (4.1)	66.3 (3.4)	14.0
	Women	12	76.9 (2.8)	71.4 (2.7)	7.2
	All	24	77.0 (2.5)	70.3 (2.2)	8.7
Chronic	Men	24	65.2 (2.6)	53.2 (2.9)	18.4
	Women	48	73.1 (1.8)	65.5 (1.5)	10.4
	All	72	70.5 (1.5)	61.4 (1.4)	12.9
Total	Men	67	71.9 (1.4)	62.8 (1.4)	12.7
	Women	116	76.1 (1.0)	69.8 (0.8)	8.3
	All	183	74.6 (0.8)	67.2 (0.7)	9.9

TABLE 3b Mean summer and winter levels of carbon monoxide (CO) (and standard errors) at three measurement sites in the houses

House measurements		Mean CO levels (ppm)			
Location	No. of houses	Summer	Winter	Difference	p-value*
Fire	73	24.5 (5.0)	64.9 (8.8)	40.4 (10.2)	<0.001
Floor	69	10.5 (1.2)	18.4 (2.4)	7.9 (2.5)	<0.01
Middle	68	14.9 (1.8)	26.2 (3.4)	11.3 (3.5)	<0.01

\*The distributions of CO in exhaled air, and particularly in the houses, are positively skewed. P-values in Tables 3a and 3b, and those relating to Table 6, are therefore derived from log-transformed data. The standard errors shown are of the untransformed values.

TABLE 5 The association between the decrease in FEV<sub>1</sub> (litres) between summer and winter in women and non-smoking men examined in both surveys, and the change in the level of carbon monoxide (CO) in exhaled air (ppm) between summer and winter

	Decrease in FEV <sub>1</sub> (in litres) according to the level of change in exhaled CO (in ppm) between summer and winter								
	<5 ppm change			5-10 ppm change			>10 ppm change		
	No.	Mean fall in FEV <sub>1</sub>	(S.E.)	No.	Mean fall in FEV <sub>1</sub>	(S.E.)	No.	Mean fall in FEV <sub>1</sub>	(S.E.)
Men	26	0.31	(0.05)	16	0.32	(0.06)	21	0.42	(0.05)
Women	35	0.08	(0.06)	28	0.16	(0.04)	48	0.23	(0.05)
Total	61	0.18	(0.04)	44	0.22	(0.03)	69	0.29	(0.04)

*The Use of Chimneys and the Level of Pollution*

A record was made during the winter survey of whether the fire (or fires) in each house were alight, and if so whether a chimney was being used (Table 6). The use of fires exclusively without a chimney (column c) was associated with higher levels of individual exhaled air CO when compared to houses using fires with a chimney (column b) ( $p < 0.01$ ), although there was a only a small difference when fires with chimneys were compared with no fire alight (column a). A similar pattern was seen for the house measurements of CO, where values for houses having fires alight exclusively without chimneys (column c) were higher at all three locations ( $p < 0.01$ ) in comparison with houses using fires exclusively with a chimney (column b). Even so, the levels of ambient CO found in houses using fires exclusively with a chimney (column b) were still considerably higher than where no fire was alight at the time of the survey (column b), particularly for measurements made close to the fire ( $p < 0.01$ ) and in the middle of the room ( $p < 0.05$ ). All  $p$ -values quoted for CO level comparisons relating to Table 6 are for the log-transformed data.

The highest CO levels were found in houses where fires both with and without a chimney were in use at the time of the survey (column d), presumably because a larger number of fires were alight in each house. These houses showed significantly higher values of CO than those where exclusively fires without chimneys were

alight (column c), but only for measurements of individual exhaled air ( $p < 0.05$ ), and of the air in the middle of the room ( $p < 0.05$ ).

## DISCUSSION

This study set out to investigate clinical impressions that the villagers of Chuchot experienced a considerable burden of chronic respiratory disease, and this appears to have been confirmed. The prevalence of chronic cough and phlegm was greater in women than men, and rose steeply with age. These chronic symptoms were both associated with reduced FEV<sub>1</sub>/FVC ratios which is suggestive of obstructive disease. When measured in summer, about one-quarter of men, and one-third of women over 50 years had evidence of obstructive disease defined as an FEV<sub>1</sub>/FVC ratio of less than 65%.<sup>9</sup> The excess of chronic cough in women as compared to men was particularly notable at age 20-29, which is similar to the findings for chronic bronchitis in Nepal.<sup>10</sup> However, the excess of chronic cough and chronic phlegm among Chuchot women compared to men was seen at all ages (Table 1 and Figure 1), so the findings on the younger subjects are unlikely to have arisen simply from bias due to the higher female response rate in this group.

This pattern of respiratory illness has a number of features in common with the Chronic Obstructive Lung Disease (COLD) described in Nepal<sup>10</sup> and in Papua New Guinea.<sup>4</sup> These include the relative pre-

TABLE 6 Mean individual expired air and ambient room levels of carbon monoxide CO (ppm) during the winter survey in houses with no fire alight, and in houses with fires alight with chimneys, without chimneys, and where more than one fire was alight and at least one had no chimney

Carbon monoxide	Characteristic of fire (or fires) alight during winter survey											
	(a) No fire alight			(b) Fire(s) only with chimney			(c) Fire(s) only without chimney			(d) Fires with and without chimney		
	No.	mean	(S.E.)	No.	mean	(S.E.)	No.	mean	(S.E.)	No.	mean	(S.E.)
Exhaled air	17	11.4	(2.0)	78	12.5	(0.9)	54	16.7	(1.7)	103	20.1	(1.0)
House:												
Fire	12	6.9	(1.5)	42	47.7	(11.0)	28	102.7	(16.9)	51	113.8	(11.7)
Floor	13	5.0	(1.2)	42	12.4	(2.5)	28	26.0	(5.0)	51	26.1	(2.1)
Middle	13	5.6	(1.3)	42	17.9	(3.7)	28	35.3	(6.6)	51	39.6	(3.1)

dominance of women being affected in comparison to Western populations, the chronic productive cough, and obstructive lung function. The respiratory disease in Chuchot was not particularly associated with smoking, indeed none of the women smoked. The independence of chronic respiratory disease from smoking is in agreement with the findings from Papua New Guinea.<sup>3,11</sup>

Other studies from Papua New Guinea<sup>12</sup> have found a similar high prevalence of chronic bronchitis with an equal sex distribution, but with some different features. There was evidence of a late onset of dyspnoea, relatively well preserved expiratory flows and severe ventilation-perfusion inequality. These findings, together with autopsy evidence suggested that fibrosis was important, probably the result of repeated respiratory infections. However, clinical examinations, more detailed lung function, and chest x-rays were not carried out in the Chuchot study, so it is not possible to comment further on the nature of the lung disease in Chuchot compared to the various populations studied in Papua New Guinea. Nevertheless, the symptoms and obstructive lung function do suggest a picture of COLD similar to that described by Anderson.<sup>4</sup>

The sex distribution of lung disease in Chuchot, and the independence from smoking, raised the strong possibility that domestic pollution was the cause. Although suspected and investigated in a number of developing countries,<sup>13</sup> the most direct evidence of a causal association comes from studies in Nepal, where the duration of exposure to smoke in the home (assessed by time spent near the stove) has been shown to be associated with symptoms of chronic bronchitis<sup>5</sup> and with lower lung function.<sup>5</sup>

The measure of pollution used in the present study is CO. Fires burning biomass fuel (wood, dung, agricultural residues) produce a range of pollutants including CO, nitrogen dioxide, suspended particulates, hydrocarbons and aldehydes.<sup>13,14</sup> The most important irritants of the lower respiratory tract are nitrogen dioxide and particulates.<sup>14</sup> Although these two products were not measured directly in Chuchot, the levels of CO detected in the houses in winter are consistent with high levels of nitrogen dioxide and particulates being present.<sup>15</sup> The CO levels have been shown to correlate highly with smoke density ( $r = 0.84$ ) in pollution from wood fires in Papua New Guinea,<sup>16</sup> and dung produces essentially similar combustion products to wood including suspended particles of respirable size.<sup>15</sup> Acute exposure to smoke from biomass fuel has been shown to cause elevated carboxyhaemoglobin levels when using traditional stoves in India.<sup>17</sup>

The marked increase in CO levels observed during

the winter in Chuchot is consistent with the expected pattern of change in pollution. Over the same period there was a highly significant fall in FEV<sub>1</sub>, but not in FVC, which suggests that pollution could be having a relatively acute obstructive effect on the lungs. The fact that the fall in FEV<sub>1</sub> was greater in those with chronic symptoms makes it unlikely that the effect was artefactual. The level of winter pollution showed no significant association with symptoms, although there was some evidence of an association with the winter FEV<sub>1</sub>/FVC ratio, particularly for women. The marked variability of CO levels in the home<sup>16,18</sup> would weaken these associations, although the exhaled CO values are less variable than the house measurements and would thus be expected to yield stronger results. However, the finding of an association between individual change in CO and individual change in FEV<sub>1</sub> between summer and winter does provide stronger evidence of a causal role for pollution.

It cannot be demonstrated here that the winter fall in FEV<sub>1</sub> is reversible, since this would have required a third (summer) study. Furthermore, although the findings in Chuchot suggest that pollution may cause a fall in FEV<sub>1</sub> over six months, this does not necessarily mean that it can lead to chronic obstructive disease. The greater fall in FEV<sub>1</sub> among those with chronic symptoms is suggestive of this, but it could also be that those who already have disease are more susceptible to the irritant effects of pollution. However, there is evidence from rats that exposure to cow dung smoke can lead to chronic bronchitis, bronchiolitis, and focal collapse with emphysema.<sup>19</sup> In humans, Pandey found evidence of lower FEV<sub>1</sub> and FVC as duration of exposure to biomass smoke increased, but this was based on a cross-sectional rather than a longitudinal design.<sup>5</sup>

The mechanism by which biomass smoke could cause COLD is not certain. Nitrogen dioxide and particulates can penetrate the lower respiratory tract and lead to irritation, ciliastasis and mucosal damage.<sup>13,14</sup> Acute exposure to particulates may cause a reduction in lung function which can persist for two to three weeks.<sup>14</sup> The risk of infection may also be increased, and this could lead to COLD as suggested by Woolcock.<sup>12</sup> It is also strongly suspected that domestic pollution is a cause of acute respiratory infections among children in developing countries.<sup>20</sup>

Other possible causes of COLD in highland communities have been discussed, including tuberculosis, asthma, and mould sensitivity.<sup>3</sup> Although there is no firm evidence, clinical impressions suggest that tuberculosis is not particularly common in Chuchot. This is consistent with observations from other highland communities such as Papua New Guinea,<sup>3</sup> and in Nepal

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where a tuberculosis prevalence of 1.3% was found among subjects with symptoms of chronic bronchitis.<sup>10</sup> To our knowledge, airways reversibility and mould sensitivities have not been studied in Ladakh, but asthma is reported by clinicians to be very rare and the dry climate might be expected to restrict fungal growth. There was no evidence from this study that cigarette smoking has yet become a major contributor to chronic respiratory illness in Chuchot, but this is likely to be due to the fact that smoking is almost entirely restricted to men under 40 years. A preliminary study of Chuchot and the nearby village of Stok has shown a high prevalence of silicosis in older people, and while more detailed investigation is required, it is possible that exposure to dust is another cause of respiratory illness.

The winter levels of pollution in the houses were, as expected, higher where no chimney was in use. The CO levels close to the fires in these houses (where women sit for long periods) were about twice the recommended time-weighted eight-hour level of 50 ppm,<sup>21</sup> but only slightly below this level (47.7 ppm) in houses where a chimney was in use. However, it is the nitrogen dioxide and particulate pollution associated with these levels of CO that is of greater importance.

We have observed that many chimneys leak, and that the embers are often raked onto an open hearth to increase space heating. There is clearly a need to improve the cooking and heating arrangements, although effective chimneys are only one aspect of efficient fire design.<sup>22</sup>

## CONCLUSIONS

It seems likely that domestic fire pollution is an important factor in the high prevalence of chronic lung disease in Chuchot, and this appears to be of particular importance for women. Further work is required to clarify whether the winter fall in FEV<sub>1</sub> is recovered in the following summer, and whether this relatively acute impairment leads on to chronic obstructive disease in the longer term. The importance of tuberculosis, other infections, airways reversibility and dust pneumoconiosis in this community also needs to be examined further. Although the demonstration of a direct association between pollution and lung function in the Chuchot study adds to the evidence for a causal link between domestic pollution and chronic lung disease, it remains a difficult case to prove. We agree with the suggestion of others that intervention studies are now required.<sup>20,23</sup> In the meantime, it is important to prevent cigarette smoking becoming more prevalent among men and being adopted by women, as this is likely to cause a further deterioration in the respiratory health of this community.

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Norboo, T., Yahya, M., Bruce, N.G., Heady, J.A., and Ball, K.P.,  
"Domestic Pollution and Respiratory Illness in a Himalayan Village,"  
International Journal of Epidemiology 20: 749-757, 1991.

The authors utilized summer and winter surveys to study respiratory illness and domestic pollution from fires in an arid high altitude region of northern India. The authors conclude that "domestic pollution is an important contributor to chronic respiratory illness in this community" and that "an intervention study is now required to establish the benefits to health of an improved fire design."

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Xu, X., Dockery, D.W., and Wang, L., "Effects of Air Pollution on Adult Pulmonary Function," Archives of Environmental Health 46(4): 198-206, 1991.

The authors conducted a study to determine potential respiratory health effects of indoor and outdoor air pollution. Lung function measurements were performed on 1440 adults who were 40-69 years of age and who had never smoked. Outdoor ambient air pollution measurements from the World Health Organization Global Air Pollution Monitoring Station were utilized. Heating with coal was reportedly associated with reduced FEV(1.0) and FVC. Living in the residential area was apparently associated with an additional reduction in FEV(1.0) and FVC. The authors reported that "after we adjusted for age, height, and sex, an inverse linear association was found" between outdoor SO<sub>2</sub> (or TSPM) concentration and FEV(1.0) and FVC in subjects who had and had not used coal stove heating. The authors concluded that "not only was coal heating an important risk factor for pulmonary function, but it was a major confounding factor in the analysis of outdoor air pollution effects."

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# Effects of Air Pollution on Adult Pulmonary Function

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**ABSTRACT.** We conducted a study in three representative areas of Beijing to determine respiratory health effects of indoor and outdoor air pollution. In August 1986, we measured the lung function of 1 440 adults who were 40–69 y of age and who had never smoked. Forced vital capacity (FVC) and forced expiratory volume in 1 s ( $FEV_{1.0}$ ) were adjusted for height, sex, and age. Outdoor ambient air pollution measurements from the World Health Organization Global Air Pollution Monitoring Station were very different in the three study areas; the annual mean concentrations of sulfur dioxide ( $SO_2$ ) in residential, suburban, and industrial areas were 128, 18, and 57  $\mu g/m^3$ , respectively, and annual mean concentrations of total suspended particulate matter (TSPM) were 389, 261, and 449  $\mu g/m^3$ , respectively. Coal was most frequently used for domestic heating in the residential (92%) and suburban (96%) areas compared with the industrial area (17%). Heating with coal was associated with a reduced  $FEV_{1.0}$  ( $-91 \pm 36$  ml) and FVC ( $-84 \pm 41$  ml). Living in the residential area was associated with an additional reduction in  $FEV_{1.0}$  ( $-69 \pm 34$  ml) and FVC ( $-257 \pm 37$  ml). After we adjusted for age, height, and sex, an inverse linear association was found between  $\ln$  outdoor  $SO_2$  (or TSPM) concentration and  $FEV_{1.0}$  and FVC in subjects who had and had not used coal stove heating. Regression analysis results showed that a per-unit increase in  $\ln$   $SO_2$  (TSPM) concentration ( $\mu g/m^3$ ) could result in a 35.6 (131.4) ml reduction in  $FEV_{1.0}$  and a 142.2 (478.7) ml reduction in FVC. Not only was coal heating an important risk factor for pulmonary function, but it was a major confounding factor in the analysis of outdoor air pollution effects.

RESPIRATORY DISEASES are the second leading cause of death in the overall population in China.<sup>1</sup> The magnitude of the problem of respiratory diseases is also well represented by a dozen massive surveys of the prevalence of respiratory diseases.<sup>2</sup> In early 1970, 2 680 957 residents in Shanghai were surveyed for bronchitis. The prevalence rate of chronic bronchitis was 3.0% for all subjects and 12.3% for those who

were at least 50 y of age. During the 1970s, a total sample of 2 507 971 residents who were more than 14 y of age were selected in 13 other communities of China. Information on history of chronic bronchitis, emphysema, and chronic cor pulmonale was obtained by special teams appointed by the Ministry of Public Health. The median prevalence rates for chronic bronchitis, emphysema, and chronic cor pulmonale were

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5.6, 1.3, and 0.4%, respectively (highest rates were 13.8, 3.2, and 1.1%, respectively).

Air pollution is thought to be one of the most important risk factors of respiratory diseases.<sup>1</sup> However, to what degree mortality and/or morbidity is attributable to air pollution remains to be estimated. Rapid urbanization and industrialization has contributed to the increasing problem of air pollution in China. Data gathered from air monitoring stations suggest that concentrations of total suspended particulate matter (TSPM) and sulfur dioxide (SO<sub>2</sub>) are high nationwide throughout the year. Higher levels of air pollutants have been found in northern cities compared with southern cities, and levels are higher during winter than summer.<sup>3,4</sup> The daily mean concentration of TSPM in 60 cities in China was as high as 660 µg/m<sup>3</sup>.<sup>5</sup> Indoor air pollution caused by coal combustion during cooking and heating, and smoking in crowded households, should not be overlooked as sources of air pollution.

This study investigated the effects of major environmental risk factors on respiratory health in adults in residential, industrial, and suburban (control) areas in Beijing, China. We focused on the relationship between air pollution and pulmonary function among adults who had never smoked. This group of adults was selected because subjects who do not smoke may be more sensitive to airborne contaminants.<sup>6</sup> Also, active smoking would not have been a confounding factor. We initially developed a prediction equation that described the relationship between pulmonary function and several demographic and body size variables, which may have served as important confounders. The model was then expanded to estimate the effects of outdoor air pollution and indoor coal combustion. The impact of cigarette smoking on pulmonary function and its interaction with age, sex, and air pollution will be investigated in subsequent reports.

## Methods

**Sites selected.** Three areas—industrial, residential, and suburban (control)—in Beijing were selected for five reasons: (1) outdoor air pollution monitoring data for these areas have been available since 1981; (2) the resident population was fairly stable; (3) the population was sufficient to ensure that sample sizes of at least 3 600 adults would be available; (4) the population did not include a large number of subjects who had been occupationally exposed to asbestos or silica, etc., thus eliminating important confounders; and (5) the ethnic mix was not too heterogeneous.

**Study population.** All subjects in the three study areas were selected from 1982 National Census Records. A two-stage random sampling technique was employed. The first stage sample unit was the administrative unit, i.e., JUWEIHUEI or village; at the second stage, it was the subject. Equal numbers of males and females were drawn from each area. Subjects were excluded if they (a) were outside the chosen age range (40 to 69 y of age), (b) were dead, (c) had moved, or (d) were a non-resident or had resided in the three study areas less than 5 y or less than 6 mo/y. Age criteria was

based on two assumptions: (1) there is a significant increase in the prevalence of chronic obstructive pulmonary disease in individuals who are 40+ y of age, and (2) it is difficult to obtain a satisfactory pulmonary function test for individuals aged 70+ y. The criteria outlined above accords with available air monitoring data.

**Assessment of health effects.** A cross-sectional survey was conducted in August 1986. A trained interviewer, who used a modified standardized questionnaire,<sup>7</sup> determined history of chest illnesses, respiratory symptoms, cigarette smoking, occupational exposure, residential history, education level, and type of fuel used for cooking and heating. Pulmonary function measurements were completed in accordance with the guidelines of the American Thoracic Society.<sup>8</sup> Subjects performed vital capacity (VC) and forced vital capacity (FVC) tests on the electric auto spirometer (AS-300, Japan) while in the standing position and with a nose clip. Tests occurred either at the central station or at the subjects' homes. A minimum of three acceptable measurements were performed. The maximum of three measurements was used because it was more reproducible than the mean,<sup>9</sup> and the "best test" was the simplest and most practical result to record.<sup>10</sup> FVC and FEV<sub>1.0</sub> values were expressed as ATPS because all pulmonary function measurements were made during August and September—times during which indoor temperature was relatively constant.

**Air monitoring.** The outdoor TSPM and SO<sub>2</sub> (1981–1985) pollution data were obtained from World Health Organization Global Air Monitoring Stations, which were located in the three study areas. Gravimetric and calorimetric pararosaniline methods were used to determine TSPM and SO<sub>2</sub>, respectively.<sup>11</sup>

**Indoor air pollution.** Because indoor coal combustion is the major source of indoor air pollution, and because there was no indoor air monitoring data available in Beijing in 1986, the presence of coal stove heating was used as a proxy for indoor air pollution in this report. Passive exposures to active cigarette smoking at home or at the office were also accounted for.

**Procedure.** In each area, three survey teams included local interviewers and a core of permanent staff who moved from site to site. Each team was further divided into three groups: (1) an air monitoring group, (2) a questionnaire interview group, and (3) a pulmonary function measurement group. The interviewers trained for 2 wk, during which time they studied the questionnaire and reviewed criteria for adequate testing of pulmonary function. Each subject who was selected received a letter that described and explained the purpose of the study. Local officials and health centers arranged for the subjects to participate in the study at the center station at a convenient time. Home visits were made for those who could not come to the center station. Questionnaire responses were reviewed by each group leader for completeness and consistency. Omitted or ambiguous items were addressed during a re-visit.

**Statistical methods.** Dockery et al.<sup>12</sup> indicated that when  $FEV_{1.0}$  and FVC measurements were standardized for height (HT), by dividing by  $HT^2$ , the decline of lung function with age among never-smokers was described by a simple linear function of age. After repeating the same exploratory procedure with our own data, we found that this method of standardization also eliminated the relationship between height and  $FEV_{1.0}$  or FVC in our sample. The same method of standardization for height adjustment was used in the data analysis. The results were made more interpretable by adjusting  $FEV_{1.0}/HT^2$  and  $FVC/HT^2$  values to the sex-specific mean height squared, i.e.,  $FEV_{1.0}/HT^2$  and  $FVC/HT^2$  were multiplied by  $(1.67\text{ m})^2$  for men and  $(1.56\text{ m})^2$  for women.

Several other stages of analysis were performed so that predictive models for pulmonary function could be derived. Bivariate plots of height-adjusted  $FEV_{1.0}$  and FVC against age (in 5-y intervals) were constructed by sex. This was done to determine the functional form of pulmonary function with age, sex, and the interaction between sex and age. Several models were then fitted by multiple linear regression. The choice of final predictive models were based on parsimonious parameters, analysis of residuals, and comparison of  $R^2$ .

Multiple linear regression techniques were used to estimate the impact of air pollution on pulmonary function. Age, sex, education level, and passive smoking were covariates to be controlled in the analysis of air pollution and coal stove heating effects. The constant term was easier to interpret because age was centered at 55 y in all regression models.

The residual analysis suggested that the variance of the regression model residuals was inconsistent for several covariates. Therefore, ordinary least squares re-

gression provided unbiased estimates of the regression coefficients, but it did not provide valid estimates of their standard errors. When the variance consistency test showed significance differences, robust estimates of the variances of the OLS estimates were calculated using methods described elsewhere.<sup>13</sup>

## Results

**Sample characteristics.** The expected sample was 1 200 persons in each area. However, a total 3 746 subjects were selected and invited to participate, and 3 590 (95.8% of the sample drawn) responded. Those who did not respond included persons who were out of town during the study period or who could not be contacted after three subsequent home visits and those who refused to participate. At the initial examination, 1 572 (43.8%) reported that they had never smoked. Demographic characteristics, passive smoking status, and type of heating used at the home of never-smokers who were in the study are shown in Table 1. The population in the industrial area tended to be younger than in the other two areas. There were obvious disparities in education level, i.e., males were much more educated than females; persons in industrial and residential areas more educated than those in the suburban area. A significant difference in type of heating was found between the industrial area and the other two areas. Central heating was used in at least 80% of the households surveyed in the industrial area, whereas more than 90% of households surveyed in the residential and suburban areas used coal stoves for heating. There were substantial differences in passive smoking status (i.e., males were much more exposed than females), and exposures occurred most frequently

Table 1.—Characteristics of Never-Smokers under Study by Sex, Age, Education Level, Indoor Coal Combustion, and Occupational Exposure

	Men						Women					
	Res.		Sub.		Ind.		Res.		Sub.		Ind.	
	n	%	n	%	n	%	n	%	n	%	n	%
Age (y)												
40-44	18	14.0	16	16.0	14	10.5	65	17.5	114	35.3	83	21.6
45-49	25	19.4	20	20.0	30	22.6	72	19.4	67	20.7	111	28.9
50-54	36	27.9	16	16.0	46	34.6	83	22.4	34	10.5	85	22.1
55-59	16	12.4	18	18.0	20	15.0	65	17.5	47	14.6	63	16.4
60-64	20	15.5	19	19.0	17	12.8	49	13.2	35	10.9	29	7.6
65-69	14	10.9	11	11.0	6	4.5	37	10.0	26	8.1	13	3.4
Education												
High school and above	94	72.9	33	33.0	80	60.2	160	43.1	74	22.9	129	33.6
Below high school	35	27.1	67	67.0	53	39.8	211	56.9	249	77.1	255	66.4
Heating												
Coal stove	118	91.5	96	96.0	22	16.5	337	90.8	297	92.0	63	16.4
Central, etc.	11	8.5	4	4.0	111	83.5	34	9.2	26	8.0	321	83.6
Passive smoking												
Yes	72	55.8	29	29.0	95	71.4	167	45.0	87	26.9	205	53.4
No	57	44.2	71	71.0	38	28.6	204	55.0	236	73.1	179	46.6

Notes: Res = residential area, Sub = suburban area, and Ind = industrial area.



in the industrial area compared with the suburban area, in which exposures were the least frequent.

**Air pollution level.** China has promulgated its Ambient Air Quality Standards (AAQS), which were revised in 1982.<sup>4</sup> The 5-y (1981–1985) mean concentrations of TSPM and SO<sub>2</sub> in the three study areas are summarized in Table 2. TSPM in all three areas was higher than WHO-recommended limits (Table 2), and it was the highest in the industrial area. The SO<sub>2</sub> concentration was the highest, and well above the AAQS- and WHO-recommended limits, in the residential area. As expected, the suburban area had the lowest concentrations of both major pollutants.

**FEV<sub>1.0</sub> and FVC relationships with age and sex.** Sex-specific mean values of height-adjusted FEV<sub>1.0</sub> and FVC, by age group, are shown in Figures 1 and 2. The height-adjusted values of men were consistently larger than values of women. The average difference was 0.70 l for FEV<sub>1.0</sub> and 0.87 liters for FVC, which was almost constant over the 40- to 70-y age range. The decline in both height-adjusted FEV<sub>1.0</sub> and FVC as age increased appeared to be close to linear for both sex groups.

These graphic analyses suggest that height-adjusted FEV<sub>1.0</sub> and FVC levels varied linearly with age, and that a difference existed between sexes that was independent of age. When this model was fitted by ordinary least squares, the resulting equations were

$$FEV_{1.0} = HT^2 \times [2.668 - 0.031 \times (AGE - 55) - 0.737 \times SEX] / (1.67^2 \text{ for men or } 1.56^2 \text{ for women})$$

and

$$FVC = HT^2 \times [3.365 - 0.035 \times (AGE - 55) - 0.910 \times SEX] / (1.67^2 \text{ for men or } 1.56^2 \text{ for women}).$$

In these equations, FEV<sub>1.0</sub> and FVC are in liters, age is in y and is centered at 55 y, and sex is 0 for men and 1 for women. The coefficient of determination (R<sup>2</sup>) for these prediction equations was 0.466 for FEV<sub>1.0</sub> and 0.508 for FVC. The standard error of the estimate (root mean squared error) was 0.474 l for FEV<sub>1.0</sub> and 0.525 l for FVC. We also considered models that included the quadratic age term, but the quadratic age coefficient was not significant for either pulmonary function value.

The height-adjusted FEV<sub>1.0</sub> and FVC data were fitted, allowing different age coefficients for each sex. No

significant differences between regression coefficients for men and women were found for either the FEV<sub>1.0</sub> or FVC models.

**Impact of air pollution and coal stove heating.** The predicted height-adjusted lung function values, FEV<sub>1.0</sub> and FVC, were calculated for each person in the sample. These calculations were completed using a model that included sex and age, and FEV<sub>1.0</sub> and FVC were subtracted from the observed height-adjusted values to produce pulmonary function residuals. The residual plots, by area, and the presence of coal stoves indicated that reduced FEV<sub>1.0</sub> and FVC were consistently associated with coal stove heating and with increased air pollution level (Figs. 3 and 4). The slope for FEV<sub>1.0</sub> for subjects who did not report using coal stove heating was steeper than for subjects who reported using coal stove heating, which suggests that the unexposed subjects may have been more sensitive to airborne contaminants. The effect of coal stove heating on pulmonary function in subjects located in the industrial area was less pronounced than in the other two areas, the major reason being that, since 1978, coal stove heating in many homes had been gradually replaced with central heating systems. The proportion of replacements was highest in the industrial area and lowest in the suburban area. The effects of coal heating in the three areas were inversely associated with the proportion of change in heating system. A stronger association was noted for FVC, which suggested that, after terminating exposure to coal stoves, FVC was less reversible than was FEV<sub>1.0</sub>. The differences in coal stove effects on both FEV<sub>1.0</sub> and FVC among the three areas and the interaction between coal heating and ln(SO<sub>2</sub>) were tested using a multiple linear regression model. However, none of these were statistically significant.

A multiple regression model of FEV<sub>1.0</sub> and FVC measurements was used to develop a unified model for sex, age, and air pollution effects. The model included age, sex, educational level, passive smoking, indoor heat type, plus residential areas or their ln SO<sub>2</sub> (or ln TSPM) concentration as regression variables.

As shown in Model 1, on average, a 69-ml and 62-ml decline in FEV<sub>1.0</sub> and a 257-ml and 177-ml decline in FVC were found in the residential and industrial areas, respectively, compared with the suburban control area

Table 2.—Annual Mean Concentration of TSPM and SO<sub>2</sub> in Residential, Industrial, and Suburban Areas, Beijing, 1981–1985

	Area			AAQS*			WHO†	
	Res.	Ind.	Sub.	I	II	III	Annual	Daily
TSPM (μg/m <sup>3</sup> )	389	449	261	150	300	500‡	60–90	150–230
SO <sub>2</sub> (μg/m <sup>3</sup> )	128	57	18	20	60	100§	40–60	100–150

Notes: Res = residential area, Ind = industrial area, and Sub = suburban area.

\*Ambient Air Quality Standard in China.<sup>4</sup>

†WHO guidelines for exposure limits.<sup>11</sup>

‡Daily mean.

§Annual mean.

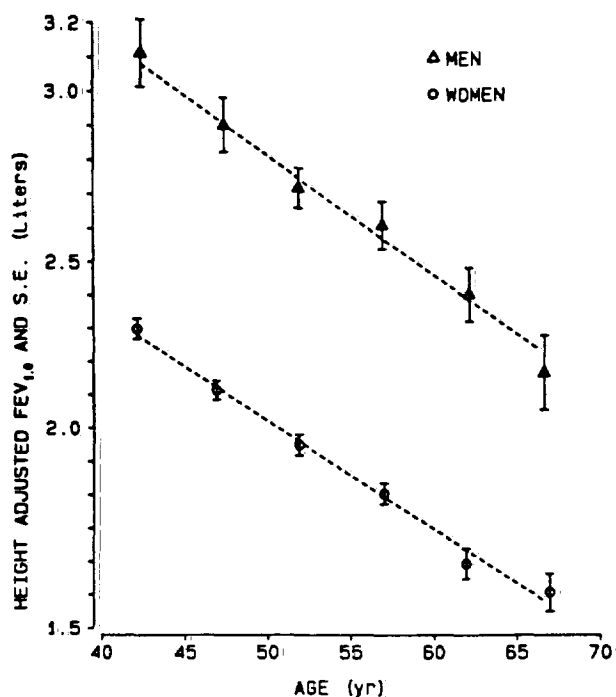


Fig. 1. Comparison of predicted and observed height-adjusted  $FEV_{1.0}$  for participants who were never-smokers. The triangles (men)/circles (women) and error bars represent the mean  $\pm$  standard error of the observed  $FEV_{1.0}$  for subjects grouped by 5-y age interval. The dashed line connects the means of the predicted values from the predictive model.

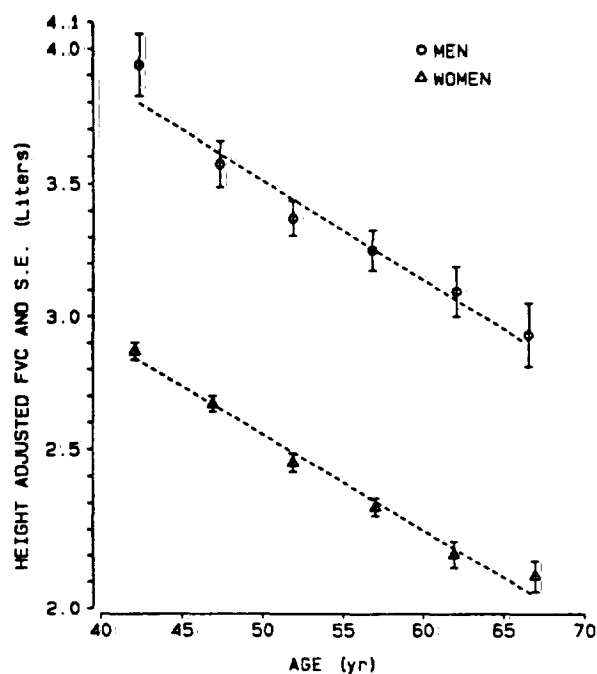


Fig. 2. Comparison of predicted and observed height-adjusted FVC for participants who were never-smokers. The triangles (men), circles (women), and error bars represent the mean  $\pm$  standard error of the observed FVC for subjects grouped by 5-y age interval. The dashed line connects the means of the predicted values from the predictive model.

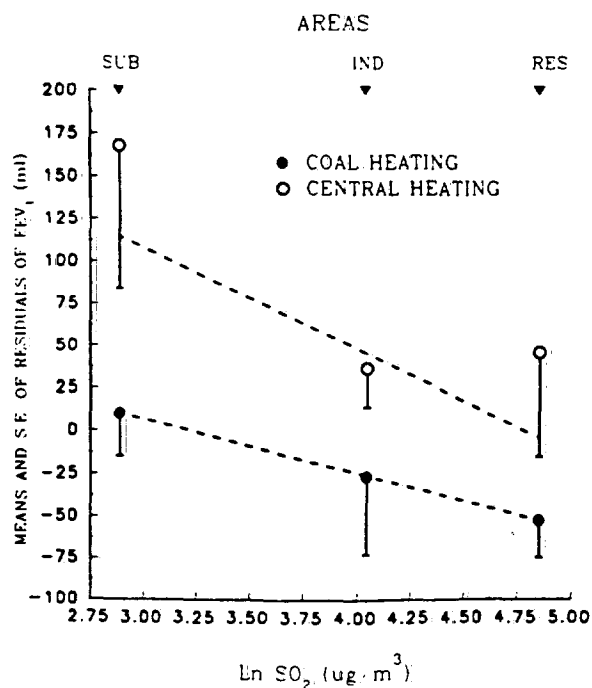


Fig. 3. Mean height-adjusted  $FEV_{1.0}$  residuals versus  $\ln$  sulfur dioxide ( $SO_2$ ) concentration ( $\mu g/m^3$ ) in residential, industrial, and suburban areas, by presence of coal stove heating.

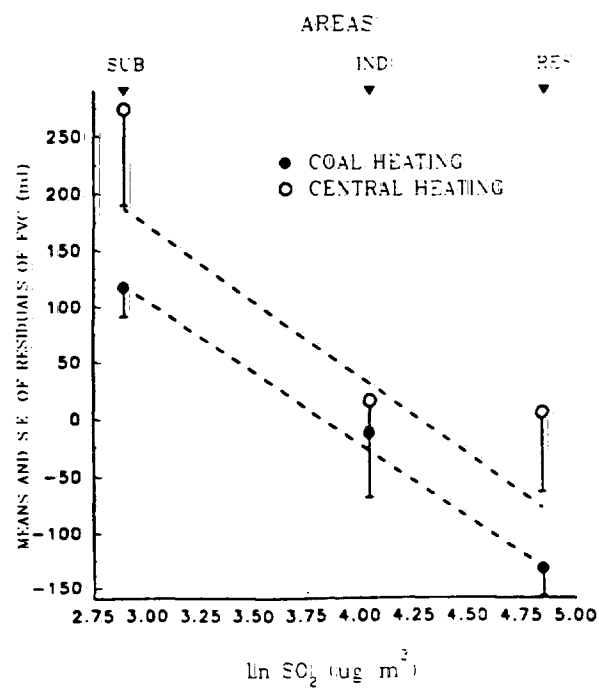


Fig. 4. Mean height-adjusted FVC residuals versus  $\ln$  sulfur dioxide ( $SO_2$ ) concentration ( $\mu g/m^3$ ) in residential, industrial, and suburban areas, by presence of coal stove heating.

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after adjusting for age, sex, educational level, passive smoking, and indoor heat type. This finding provided an important explanation of why the residential area was associated with the worst pulmonary function. Coal stove heating was found to be independently associated with a 91-ml reduction in  $FEV_{1.0}$  and an 84-ml reduction in FVC. In Models 2 and 3, the  $\ln$  concentration of  $SO_2$  and TSPM in each area replaced the dummy variables. A per  $\ln$  unit ( $\mu g/m^3$ )  $SO_2$  increase could result in a 35.6-ml reduction for height-adjusted  $FEV_{1.0}$  and a 131.4-ml reduction for FVC. The estimates of a per  $\ln$  unit ( $\mu g/m^3$ ) TSPM were 4.0 and 3.6 times larger than  $SO_2$  for  $FEV_{1.0}$  and FVC, respectively (Table 3). Reduction in FVC was consistently much greater than in  $FEV_{1.0}$ .

**Variance estimation.** The standard errors in Table 3 were estimated by the robust methods described previously. Ordinary least squares estimates and robust methods gave identical estimates for regression coefficients but provided different estimates of standard errors and different values for test statistics. The differences between the robust and ordinary least squares estimates of standard errors were small in this data setting. For example, in Model 1, ordinary least squares regression gave standard errors of 40.2, 44.0 and 33.1 for the parameters of coal stove heating, industrial area, and residential area, respectively, which corresponded to 110%, 107%, and 98%, respectively, of the standard errors obtained by robust methods.

## Discussion

China is a vast country with significant variations in geographic conditions, socioeconomic development,

and industrialization across different regions. As a result, the type, level, and source of air pollution varies enormously from region to region. On the other hand, residential populations are quite stable. All these afford unequalled, wide-scope<sup>1</sup> natural experimental fields with which to study the health impacts of various types and levels of pollutants.

In this study, three representative areas in Beijing were selected. Beijing is the capital of the People's Republic of China and has a population of more than 10 million. It is also the political, economic, and cultural center of the country. Prior to the 1950s, Beijing was a nonindustrial city. Subsequent to that time, light and heavy industry gradually emerged, e.g., steel plants, petroleum refineries, chemical plants, electric power plants, etc. There are three major sources of air pollution in Beijing: (1) industrial emissions, (2) residential heating and cooking, and (3) natural sources, e.g., wind. Suspended particulate matter and sulfur dioxides are the two major pollutants. Nitrogen oxides have not been considered to be a serious contributor to the environmental problem.

Beijing experiences four distinct seasons. Natural soil dust wind comes from the far north in dry air, especially in winter and spring. A general survey conducted in Beijing showed that natural dust contributed to 40% of the TSPM in winter and 60% in the summer.<sup>14</sup> Even though we specifically examined the association between pulmonary function and outdoor TSPM pollution level in this study, a cautious interpretation should be made. Particle size and composition have been implicated as important determinants of particle toxicity,

Table 3.—Multiple Regression Estimates (Standard Errors) for 1 440 Never-Smoking Adults (Age Centered at 55 y)

	Height-adjusted $FEV_{1.0}$ (ml)*			Height-adjusted FVC (ml)*		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Constant	2 798.4 (52.8)	2 885.0 (83.5)	3 600.0 (418.7)	3 611.6 (58.4)	3 971.7 (91.1)	6 330.6 (459.7)
[AGE-55] (y)	-30.4 (1.9)	-30.3 (1.8)	-30.6 (1.8)	-32.6 (2.0)	-32.5 (2.0)	-33.9 (2.0)
Sex (1 = female)	-734.6 (33.6)	-733.9 (33.6)	-736.3 (33.6)	-907.2 (37.4)	-906.3 (37.5)	-916.5 (37.6)
Education level (1 = below high school)	-21.6 (30.1)	-23.0 (30.0)	-17.1 (28.9)	-34.5 (33.3)	-36.2 (33.1)	-10.4 (32.1)
Passive smoking (1 = yes)	-24.4 (25.8)	-25.4 (25.7)	-25.0 (25.7)	-31.9 (28.3)	-33.1 (28.3)	-35.2 (28.4)
Heating type (1 = coal stove)	-90.9 (36.4)	-75.2 (26.2)	-108.0 (30.3)	-83.6 (41.3)	-64.5 (28.5)	-174.4 (33.8)
Residential area (1 = yes)	-69.2 (33.9)			-257.1 (37.0)		
Industrial area (1 = yes)	-61.5 (41.1)			-176.5 (46.2)		
$\ln SO_2$ ( $\mu g/m^3$ )		-35.6 (17.3)			-131.4 (18.8)	
$\ln TSPM$ ( $\mu g/m^3$ )			-142.2 (68.6)			-478.7 (75.4)
$R^2$ †	0.471	0.471	0.471	0.530	0.530	0.526

\*Height-adjusted  $FEV_{1.0}$  (ml) equals observed  $FEV_{1.0}$  divided by height squared times  $(1.67 \text{ m})^2$  for men and  $(1.56 \text{ m})^2$  for women.

† $R^2$  is squared correlation between predicted and observed  $FEV_{1.0}$  and FVC.

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but TSPM itself did not reveal any distinction in terms of size and composition. The proportion and components of respirable particles varied greatly during different seasons and different areas. Sulfur dioxide emissions, however, resulted primarily from coal combustion. Coal was the dominant energy source in China for many years, and it contributed more than 70% of total energy production.<sup>15</sup> Currently, approximately 18 million tons of coal are burned each year. Nearly half of the coal consumed is burned in the cities, in small boilers and household stoves for heating and cooking. It is burned with low thermal efficiency, no desulfurization, inefficient dust collection, and low smokestacks. The seasonal variations in TSPM and  $\text{SO}_2$  concentrations (Figs. 5 and 6) indicated that coal combustion for heating in households was an important source of air pollution in Beijing. However, in the past several decades, the residential area was thought to be a good area to live and that only the industrial area experienced pollution. One of the striking findings in this study was that  $\text{SO}_2$  concentration in the residential area was worse than that in the industrial area. A significantly higher proportion (80%) of coal stoves for heating in the residential area compared with the industrial area (30%), and a higher population density in the residential area, may partially explain this finding.

Coal stoves for heating were used as a proxy for indoor air pollution because no data were available on indoor pollution, and coal stoves were thought to be the major source of indoor air pollution. Another advantage of this approach was that the information obtained was highly reliable (i.e., the interviewer was requested to check the central heating facility, if it was reported) and extremely economical because it was collected simultaneously with other information in the questionnaire. Coal stove cooking, however, was not a good index for indoor air pollution exposure because

(a) from spring to autumn, doors and windows were kept open in most Beijing households, and the difference in air pollution levels between indoor and outdoor settings would be very small; and (b) in 58% of the households in our sample, the kitchen was separated from the bed/living room during winter (96% during summer). Therefore, even in the winter, during which time all doors and windows are closed, a person, in whose home a coal stove is used for cooking, may not be exposed to cooking coal combustion emissions if he or she does not enter the kitchen. However, during the cold seasons, the coal burning stove for heating was usually placed in the living/bed room where every member in the house was exposed to the air pollutants emitted from it. Therefore, in this report, the coal stove for heating was chosen to represent indoor air pollution exposure. This approach, however, did not afford quantitative information. Also, since 1978, coal stove heating in many homes was gradually replaced with central heating systems. The proportion of replacements was not uniform, i.e., the greatest number of replacements occurred in the industrial area, and the smallest number occurred in the suburban area. The differences in coal effects on  $\text{FEV}_{1.0}$  and FVC among residents of the three areas indirectly reflected this uneven characteristic. Furthermore, the slope for  $\text{FEV}_{1.0}$  in subjects who did not report coal stove heating was steeper than that in subjects who reported coal stove heating, which suggested that unexposed subjects were more sensitive to airborne contaminants. However, all of these differences were not statistically significant.

To our knowledge, this is the first community-based respiratory epidemiologic study in China that has used a standardized method. To date, there has been no normal model that describes the association of  $\text{FEV}_{1.0}$  and FVC with age, sex, and height. It is, therefore, important to develop a basic model for later studies of impor-

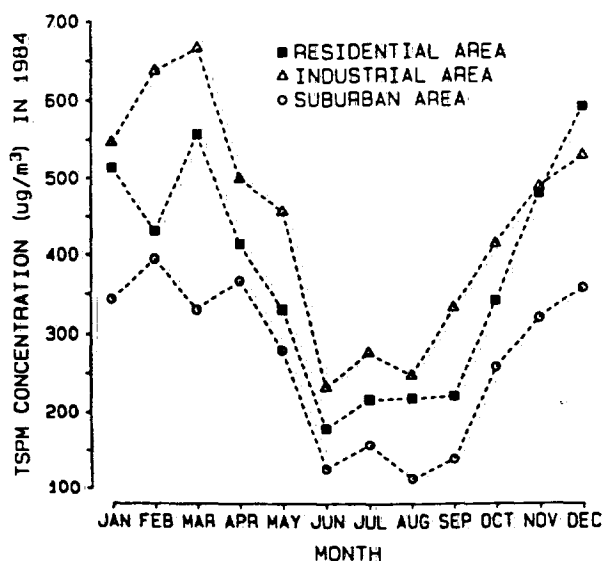


Fig. 5. Seasonal variation of total suspended particulate matter concentration ( $\mu\text{g}/\text{m}^3$ ) in residential, industrial, and suburban areas.

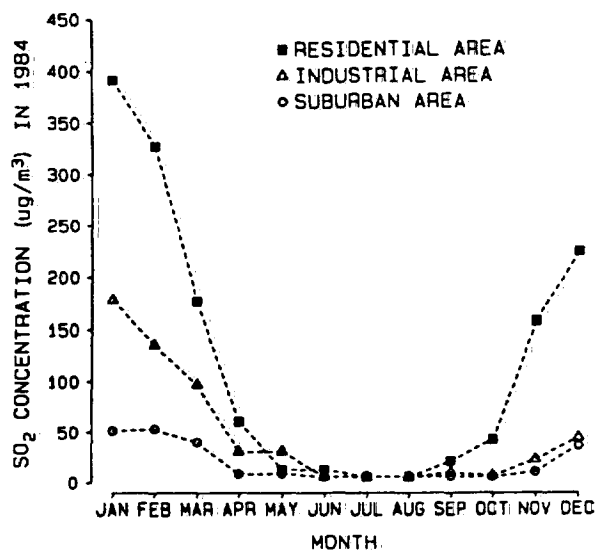


Fig. 6. Seasonal variation of sulfur dioxide ( $\text{SO}_2$ ) concentration ( $\mu\text{g}/\text{m}^3$ ) in residential, industrial, and suburban areas.

tant environmental risk factors in the Chinese population. In 1846, Hutchinson<sup>16</sup> described the relationship between mean vital capacity (VC) and height, weight, and age from measurements obtained from 1 775 healthy men. Since that time, many models for "normal" VC and other measures of pulmonary function were presented. Most models for normal values assumed a simple linear relationship between pulmonary function measurements and height and age. Recently, Dockery et al.<sup>12</sup> showed that nonlinear models were necessary to describe the transition from maximal-obtained lung function in early adult life to lower function in later life. We attempted to develop predicted models for FEV<sub>1,0</sub> and FVC measured in this sample of 1 440 Chinese adults who were (a) 40 to 70 y of age, (b) residents of Beijing, and (c) never-smokers. Our study confirms that the height-standardized method developed by Dockery et al. well described pulmonary function in this Chinese population. This method had the added advantage that, after standardizing by height squared, it was possible to describe the distribution of pulmonary function values by a two-dimensional display of adjusted pulmonary function values versus age. Our graphic analyses suggest that height-adjusted FEV<sub>1,0</sub> and FVC levels varied linearly with age (from 40 to 70 y), and that a difference between sexes, independent of age, existed. As a result, a linear model was fitted by least squares to the height-adjusted FEV<sub>1,0</sub> and FVC. We also considered models that included a quadratic age term, but the quadratic age coefficient was not significant in this age range.

Differences between the sexes in the aging terms of the model were also not significant for both FEV<sub>1,0</sub> and FVC. This suggested that once aging began, decline in pulmonary function proceeded at the same rate in men as in women, at least in these height-standardized units. Several investigators have noted that the difference in aging between sexes was related to the age at which decline began, and it would be necessary to have separate models for the periods before and after the age at which maximal lung function occurs.<sup>17,18</sup> Our data were limited to age 40 to 70 y; therefore, it would have been inappropriate to extrapolate predictions beyond the age range of this sample. Given that no predictive model for pulmonary function in the Chinese adult population has ever been available and that our study sample was selected randomly, this predictive model may also serve as a reference normal model for Beijing adult residents.

A possible confounding effect of occupational exposure on the regression estimates was also investigated. Information on occupational exposure, collected from modified ATS-DLD questionnaires, included a history of exposure to dust and fumes or gases and specific type, duration, and intensity of exposures. When the occupational exposure variables were added to the regression model, the changes in the coefficients and standard errors were negligible.

Two important findings surfaced from our regression analysis. (1) A per ln unit ( $\mu\text{g}/\text{m}^3$ ) SO<sub>2</sub> increase could result in a 35.6-ml reduction for height-adjusted FEV<sub>1,0</sub> and a 131.4-ml reduction for FVC. The estimates of a

per ln unit ( $\mu\text{g}/\text{m}^3$ ) TSPM were 4.0 and 3.6 times larger than SO<sub>2</sub> for FEV<sub>1,0</sub> and FVC, respectively. The estimated effect should not be interpreted as a unique contribution from a single pollutant because SO<sub>2</sub> and TSPM are strongly correlated. (2) Use of a coal stove for heating was found to be independently associated with a 91-ml reduction in FEV<sub>1,0</sub> and an 84-ml reduction in FVC. These findings suggested that both indoor and outdoor pollutants had significant effects on pulmonary function in this population. However, the effects found in this study were cross-sectional and cumulative, and a longitudinal study is needed to quantify the association of these pollutants with decline of pulmonary function.

There was a substantial difference in heating type between the industrial area and the other two areas (Table 1). Thus, use of coal stove heating was not only a risk factor for pulmonary function, but it was an important confounding factor to be controlled in the analysis of outdoor air pollution effects. For example, if Model 1 in Table 3 did not include coal stove heating as a controlling variable, the estimated effects of the industrial area would have been 6.2 ml for height-adjusted FEV<sub>1,0</sub> and -114.2 ml for height-adjusted FVC. Therefore, this model would underestimate the outdoor air pollution effects by more than 60 ml.

As noted previously, the association of outdoor air pollutants with FVC was constantly much stronger than with FEV<sub>1,0</sub>. There was great seasonal variation in air pollutant levels in the areas studied (Figs. 5 and 6). The mean concentration of SO<sub>2</sub> in the residential and industrial areas was as high as 392 and 178  $\mu\text{g}/\text{m}^3$ , respectively, during January, but it decreased to as low as 6  $\mu\text{g}/\text{m}^3$  during August in the same year. We tested pulmonary function during the period that the SO<sub>2</sub> level was the lowest. Therefore, the results we observed in our study reflected a longterm (i.e., chronic) effect. Fletcher et al.<sup>9</sup> studied a group of working men in London, prospectively over 10 y, and noted that there was a regular seasonal change in FEV<sub>1,0</sub>, i.e., higher values obtained in the two summer surveys than in the winter surveys. Respirable particles could produce inflammatory changes in small airways, which could be reflected in reduced lung function, particularly in reduced FEV<sub>1,0</sub> (acute or short-term effect). But there is no solid evidence that these changes necessarily proceed to irreversible changes. A greater decrement in FVC than in FEV<sub>1,0</sub>, which was observed in our study, suggested that FEV<sub>1,0</sub> was more reversible than FVC after exposure to high levels of air pollutants was terminated. Therefore, FEV<sub>1,0</sub> might be a better health index for short-term (acute) effect, whereas FVC might provide a better health index for long-term (chronic) effects in adults. The study on air pollution effects that was conducted in Berlin, New Hampshire, also maintained that SO<sub>2</sub> and TSPM were much more strongly associated with FVC than with FEV<sub>1,0</sub>.<sup>19</sup>

Studies on the effects of chronic exposure to SO<sub>2</sub> and particulates in adults have been conducted extensively. Areas of higher SO<sub>2</sub> and particulate pollution have been associated with more respiratory symptoms, an increase in bronchitis, and a lowered FEV<sub>1,0</sub> level.<sup>20,21</sup> These effects have been seen in nonsmokers but are

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more prominent in smokers. Data from the Berlin, New Hampshire, study indicated that reduction in these pollutants may be followed by some improvement in pulmonary function and an alleviation of symptoms of chronic bronchitis.<sup>22</sup> However, few of the studies provided data on the quantitative relationship between air pollution and adult pulmonary function.

Coal is the dominant energy source in China, and it will be used for many years to come. Coal consumption in cities is estimated to increase 30% by the year 2000. Coal will probably continue to be the major source of air pollution, and it may produce more excess morbidity and mortality from chronic obstructive pulmonary disease and other air pollution-related diseases. These diseases will significantly increase patient loads in hospitals and other health-care facilities, escalate China's health care costs, and reduce industrial and agricultural productivity. Air pollutants emitted from coal combustion in households have exceeded those from industrial resources, and therefore, control of air pollution is of great public health importance in these areas. There is a great need for better technology and better public policy to help prevent the enormous suffering and human loss associated with air pollution.

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Pilotto, L.S., and Douglas, R.M., "Indoor Nitrogen Dioxide and Childhood Respiratory Illness," Aust J Public Health 16: 245-250, 1992.

The authors of this review paper examine "the available evidence of this association and explore methodological issues in measurement of nitrogen dioxide exposure -- misclassification of subjects, symptom bias and confounding." The authors suggest that additional research, using personal monitoring and prospective data collection techniques, be conducted before any definitive conclusions can be drawn.

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# Indoor nitrogen dioxide and childhood respiratory illness

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**Abstract:** Nitrogen dioxide is produced from the combustion of fossil fuels and as an emission from gas-fired appliances, and is also a component of tobacco smoke. Nitrogen dioxide has been shown in experimental animals to be toxic to the respiratory tract. A number of recent studies have suggested that children exposed to significant levels of nitrogen dioxide in the home may be more susceptible to respiratory illness than children exposed to normal ambient levels. Respiratory illness is a major cause of morbidity in children everywhere. Here, we review the available evidence of this association and explore methodological issues in measurement of nitrogen dioxide exposure—misclassification of subjects, symptom bias and confounding. It has recently been shown that some New South Wales school rooms, where unflued gas heaters are often used as a source of warmth, have nitrogen dioxide levels which are above recommended ambient levels for outside air. This has underlined the need for setting standards for indoor levels of various pollutants, and cohort studies are suggested, to include personal monitoring and prospective data collection techniques. (*Aust J Public Health* 1992; 16: 245–50)

In Australia it has been reported that for children younger than 15, there were 34 recent respiratory illnesses for every 100 children and over 40 per cent of children had consulted a doctor for acute respiratory infection within a two-week period.<sup>1</sup> Also, children under five years living in urban areas were shown to have experienced an average of seven episodes of respiratory infection annually, resulting in three doctor visits a year and the restriction of activity and ingestion of medicines on 15 days per year—at an estimated cost of \$50 million.<sup>2</sup> The consequences of acute respiratory illnesses are obviously significant.

Samet has suggested identifying risk factors for these types of illnesses in order to reduce their resultant burden by appropriate interventions.<sup>3</sup> Experimental studies in animals have shown that exposure to low levels of nitrogen dioxide (NO<sub>2</sub>), of 0.3 to 0.5 parts per million (ppm), over prolonged periods (particularly in mice) increases susceptibility to experimental infection.<sup>4</sup> It follows that NO<sub>2</sub> should be considered a potential risk factor in humans.

Nitrogen dioxide is an air pollutant formed by the oxidation of nitric oxide (NO).<sup>5</sup> The major source of ambient pollution is combustion of fossil fuels, while tobacco smoke and gas-fired appliance emissions provide the main indoor source.<sup>6</sup>

This report will focus on the epidemiological evidence of association between NO<sub>2</sub> exposure and respiratory symptomatology and infection in children, who are likely to be more susceptible to air pollution than adults.<sup>7,8</sup> The current Australian experience is reviewed and recommendations for future direction are given.

## Childhood epidemiological studies

Ambient (i.e. outdoor) NO<sub>2</sub> levels, gas cooking at home, and indoor NO<sub>2</sub> levels have all been used as measures of NO<sub>2</sub> exposure in children. Studies of the association between such exposure and respiratory symptom and illness have yielded mixed results.

## Ambient (outdoor) NO<sub>2</sub> exposure studies

As shown in Table 1, all studies which relied on ambient NO<sub>2</sub> levels as measures of exposure found a positive relationship.

Shy and colleagues, in a longitudinal study using bi-weekly postcards to determine illness history, found an excess of respiratory illness in second grade school children exposed to a high level of ambient NO<sub>2</sub>.<sup>9</sup> This study is referred to as the Chattanooga School Children Study.

Pearlman and co-workers used a retrospective questionnaire in 3 217 children to determine the presence of bronchitis, croup and pneumonia over the previous three years. Bronchitis only was found to be significantly increased in first and second grade school children exposed to elevated ambient NO<sub>2</sub> levels during that period.<sup>10</sup>

Mostardi et al., using both a cross-sectional study design involving a modified Tucson Longitudinal Population Study Questionnaire and a longitudinal design with daily diaries to record symptom occurrence, found a higher incidence of respiratory symptoms in the more highly polluted areas.<sup>11,12</sup> Sulphur dioxide (SO<sub>2</sub>) was also reported to be high in the more highly polluted areas.

Love and co-workers replicated the Chattanooga study using a longitudinal design and found increased respiratory illness in children in areas more exposed to pollution. However they made the point

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Table 1: Ambient (outdoor) nitrogen dioxide studies

Design	NO <sub>2</sub> exposure	Symptom measure	Results	Reference
Longitudinal 987 children in 968 families	Ambient average concentration 0.043 ppm to 0.109 ppm	Bi-weekly postcard; phone call if new cold or sore throat	Excess illness in children exposed to high NO <sub>2</sub> areas	Shy et al. <sup>9</sup>
Cross-sectional 3 217 infants or first- and second-grade school children	Ambient average concentration 0.043 ppm to 0.083 ppm for 2 to 3 years	Questionnaire for bronchitis, croup and pneumonia, i.e. lower respiratory tract infection	Bronchitis increased in children and infants exposed to elevated NO <sub>2</sub>	Pearlman et al. <sup>10</sup>
Cross-sectional 299 children aged 10 to 11 years	Ambient average concentration 0.014 ppm to 0.027 ppm	Questionnaire based on Tucson Longitudinal Population Study questionnaire	Higher symptoms associated with polluted areas (NO <sub>2</sub> ) and SO <sub>2</sub>	Mostardi et al. <sup>11</sup>
Longitudinal, as above	As above	Daily diaries used for symptoms; given by teachers	Higher incidence of cough, sore throat and runny nose in more highly polluted areas	Mostardi et al. <sup>12</sup>
Longitudinal 2 727 children and adults	Ambient 24-hour, mean concentration 22 to 91 µg per m <sup>3</sup>	Bi-weekly phone data for symptoms	Excess respiratory illness in children in higher NO <sub>2</sub> areas	Love et al. <sup>13</sup>
Longitudinal 4 898 children aged 0 to 12 years	Ambient mean NO <sub>2</sub> of 0.049 ppm	Bi-weekly phone data for symptoms and illness	A U-shaped relation was found for illness and NO <sub>2</sub> concentration	Harrington et al. <sup>14</sup>
Longitudinal N ranged from 304 to 701 on a yearly basis	Ambient mean NO <sub>2</sub> of 0.02 to 0.06 mg/day/100 cm <sup>2</sup>	Questionnaire every summer for symptoms	Symptoms more prevalent in children more heavily exposed to pollution including NO <sub>2</sub> and SO <sub>2</sub>	Kagamimori et al. <sup>16</sup>

that it was not possible to attribute illness excess to specific pollutants.<sup>13</sup>

Harrington and Krupnick, using bi-weekly telephone data for symptoms and illness in children aged up to 12 years, found a U-shaped relationship between ambient NO<sub>2</sub> levels and respiratory illness.<sup>14</sup> No explanation has been found for this unique result. It has not been replicated in other studies and would appear to be biologically implausible, since increasing illness occurrence would be expected with increasing levels of exposure. However Abramson and Voigt have suggested that if such a curve were to exist, this could account for some of the negative findings when dichotomous exposure categories have been used.<sup>15</sup>

Kagamimori and colleagues found a higher prevalence of respiratory symptoms in atopics (children with a positive reaction to house dust extract) and school children more heavily exposed to air pollution which included both NO<sub>2</sub> and SO<sub>2</sub>.<sup>16</sup>

#### Gas cooking exposure studies

In the studies using gas for cooking at home as a measure of NO<sub>2</sub> of exposure, mixed results were found (see Tables 2a and 2b). These studies mainly involved cross-sectional study designs with retrospective parental questionnaires to determine symptom and illness histories.

Melia<sup>17,18</sup> and Florey<sup>19</sup> and their colleagues found a positive relationship between gas cooking at home and respiratory symptoms and illness. Melia's earlier study did not control for parental smoking, but this was corrected in later studies.<sup>17</sup> Speizer and co-workers, using physician-diagnosed bronchitis

and a history of serious respiratory illness before the age of two years, found a significant association between gas cooking and respiratory illness in the under-two age group.<sup>20</sup> Dodge employed a modified Tucson Longitudinal Population Study questionnaire for asthma, sputum, cough and wheeze. The prevalence of cough only was found to be significantly higher in homes which used gas cooking.<sup>21</sup> Ekwo et al. found that hospitalisation for respiratory illness before the age of two was positively associated with gas cooking at home. Such an association was not found for coughs with colds in children.<sup>22</sup> Houthuijs found an increased prevalence of respiratory symptoms associated with the use of unvented geysers in the kitchen<sup>23</sup>, while Melia found a positive association in certain ethnic groups, namely Afro-Caribbeans and whites.<sup>24</sup>

In contrast to these studies, some have found no such positive association. Keller and co-workers, following a 12-month longitudinal study involving 441 families, found gas cooking was not associated with an increase in respiratory illness in either adults or children.<sup>25</sup>

Of particular significance, Ware and colleagues expanded the cohort used in Speizer's study and found no association between respiratory illness before the age of two and gas cooking at home, and acknowledged that the literature was inconsistent regarding the health effects of gas stoves.<sup>26</sup> Harrington et al. found no association between gas cooking and respiratory illness, which was inconsistent with the results of their ambient NO<sub>2</sub> exposure trial.<sup>14</sup> Similarly, Ogston and colleagues found no association between gas cooking at home and hospitalisation and illness in the first year of life.<sup>27</sup>

*Indoor NO<sub>2</sub> monitoring studies*

Mixed results have also occurred in the few studies that measured indoor NO<sub>2</sub> levels and attempted to estimate personal levels of exposure. Florey et al. found a positive association of respiratory illness prevalence with NO<sub>2</sub> exposure (as they had also found for gas cooking) which increased with higher bedroom levels.<sup>19</sup> Houthuijs and co-workers, in the study previously reported, also found a positive relationship of prevalence of respiratory symptoms with estimated personal exposure levels of NO<sub>2</sub>.<sup>23</sup> Berwick and colleagues, using a prospective design, found an increase in symptoms of the lower respiratory tract in children aged under seven exposed to more than 0.015ppm of NO<sub>2</sub>. However this study included only 121 children, making extrapolation to the population in general difficult.<sup>20</sup> Neas et al., using

Palmes diffusion tubes to estimate mean annual household NO<sub>2</sub> exposure, found that a 15 parts per billion (ppb) increase in the mean exposure level was associated with an increased cumulative incidence of lower respiratory tract symptoms.<sup>29</sup>

Four other studies, however, have found no such positive relationship. Melia and researchers detected no significant relationship between average measured NO<sub>2</sub> levels in bedrooms and living rooms and respiratory illness.<sup>30</sup> This result was contrary to their original findings using gas cooking as a measure of exposure.<sup>17,18</sup> They discounted high humidity or low temperature as being responsible for the discrepancy.

Hoek et al., using Palmes tubes and activity data to determine personal exposure in a case-control study,

Table 2a: Gas cooking vs non-gas cooking at home—studies where positive associations were found

Design	Symptom measure	Results	Reference
Cross-sectional 5758 children aged 6 to 11 years	Retrospective questionnaire for symptoms in the previous year—smoking not controlled	Excess cough, colds going to the chest and bronchitis in gas-cooking homes	Melia et al. <sup>17</sup>
Cross-sectional (N = 4827) and longitudinal (N = 2408) Children aged from 5 to 11 years	Questionnaire as above but smoking was included	Relative risk was variable, but mostly an increased risk of one or more symptoms with gas cooking	Melia et al. <sup>18</sup>
Cross-sectional 808 children aged 6 to 17 years	Symptom Questionnaire based on Medical Research Council Questionnaire (MRCQ)	Positive association between gas cooking and respiratory illness	Florey et al. <sup>19</sup>
Cross-sectional 8120 children aged 6 to 10 years	Questionnaire for doctor for diagnosis of bronchitis and history of serious respiratory illness before age 2 and in the previous year	Significant association between gas cooking at home and respiratory illness before the age of 2 years	Speizer et al. <sup>20</sup>
Cross-sectional 676 children aged 8 to 12 years	Questionnaire for asthma, sputum, cough and wheeze	Prevalence of cough was significantly associated with gas cooking	Dodge <sup>21</sup>
Cross-sectional 1138 children aged 6 to 12 years	Used a modified American Thoracic Society Questionnaire (ATSQ)	Hospitalisation before the age of 2 was associated with gas cooking at home	Ekwo et al. <sup>22</sup>
Cross-sectional 630 children aged 6 to 9 years	World Health Organisation Questionnaire for respiratory symptoms	Gas use at home associated with an increased prevalence of respiratory symptoms	Houthuijs et al. <sup>23</sup>
Cross-sectional 4815 children aged 5 to 11 years	Retrospective questionnaire for respiratory symptoms in ethnic groups	All respiratory conditions (except asthma) were most prevalent in Afro-Caribbeans and whites	Melia et al. <sup>24</sup>

Table 2b: Gas cooking vs non-gas cooking at home—studies where no associations were found

Design	Symptom measure	Results	Reference
Longitudinal 1952 adults and children	Bi-weekly phone data from each household	No association found between gas cooking and respiratory illness in children or adults	Keller et al. <sup>25</sup>
Cross-sectional 4070 children aged 5 to 14 years	American Thoracic Questionnaire for respiratory symptoms and illness (ATSQ)	No significant association between gas cooking and symptoms of illness	Schenker et al. <sup>7</sup>
Longitudinal 4898 children aged up to 12 years	Bi-weekly telephone data for symptoms and illness	Respiratory illness was not related to gas cooking at home	Harrington et al. <sup>14</sup>
Cross-sectional 10106 children aged 6 to 9 years	Retrospective questionnaire for symptoms and illness	No significant relation between respiratory illness and gas cooking at home	Ware et al. <sup>26</sup>
Longitudinal 1565 infants in their first year of life	Hospitalisation and recall of symptoms in the previous year	No significant association was found but trends did occur	Orgston et al. <sup>27</sup>

found no difference in exposure between cases reported to suffer from bronchitis, asthma, frequent coughs or colds, and allergy, and controls.<sup>31</sup> Koo and co-workers used passive diffusion badge-style monitors worn for 24 hours to measure personal NO<sub>2</sub> exposure. They reported these monitors as having an accuracy of plus or minus 20 per cent when compared to other recognised forms of monitoring. Monitoring was conducted during one week only for each subject and no association was found between the children's NO<sub>2</sub> exposure levels and respiratory symptoms.<sup>32</sup> Dijkstra and colleagues estimated weekly average NO<sub>2</sub> concentrations at home using Palmes diffusion tubes as a measure of exposure. No association between NO<sub>2</sub> home exposure and respiratory symptoms was found.<sup>33</sup>

### Methodological issues

Concerning ambient monitoring as a measure of NO<sub>2</sub> exposure, Mostardi points out that it is difficult to determine which ambient pollutant is responsible for an effect.<sup>11</sup> More specifically, the Chattanooga study<sup>9</sup> has been criticised for presuming to distinguish the relative exposure contribution of NO<sub>2</sub> from other pollutants.<sup>5</sup> In studies measuring ambient NO<sub>2</sub> levels only, caution is needed in interpreting a positive association between polluting gases and respiratory illness to NO<sub>2</sub>.

Some authors consider that use of gas for cooking as a measure of NO<sub>2</sub> exposure leads to misclassification of subjects.<sup>25,28,34</sup> Samet and colleagues indicate that if an association is small it may not be detected because of misclassification. They believe that no definitive statement is possible concerning the risk of NO<sub>2</sub> posed by gas cooking at home.<sup>34</sup>

In most retrospective studies, questionnaires answered by parents were used to determine children's illness histories. These questionnaires were subject to bias introduced by the state of the child at the time of the questionnaire<sup>20,34</sup> and the parents' lack of knowledge.<sup>20</sup> Another source of bias relates to which parent completed the questionnaire, with fathers reporting respiratory symptoms and illness less frequently than mothers—a factor uncontrolled in past studies.<sup>7</sup>

Confounding, the effect of other variables which may be associated with the factors being studied, needs to be considered. Confounders may cause an overestimate, underestimate or may even change the direction of a true association between exposure and disease.<sup>35</sup> Potential confounders include smoking, asthma, and socio-economic status, which have not been accounted for with consistency in the reported studies.<sup>34</sup>

Table 3: Indoor nitrogen dioxide measurement

Design	Mean NO <sub>2</sub> measure	Symptom measure	Results	Reference
Cross-sectional 808 children aged 6 to 11 years	0.018 ppm to 0.122 ppm, diffusion sampling in kitchens and bedrooms	Symptoms based on Medical Research Council Questionnaire (MRCQ)	Positive association which increased with higher NO <sub>2</sub> levels	Florey et al. <sup>19</sup>
Cross-sectional 630 children aged 6 to 9 years	Palmes tube and nine budgeting for personal exposure 0.103 ppm	World Health Organisation Questionnaire for respiratory symptoms (WHOQ)	Personal exposure was associated with higher symptom prevalence	Houthuys et al. <sup>23</sup>
Longitudinal 121 children aged less than 7 years	Passive diffusion monitoring 6-90 µg/m <sup>3</sup> 0.03 to 0.045 ppm	Bi-weekly phone calls for symptoms and lower respiratory illness (LRI)	Increased LRI risk in children less than 7 exposed to 30 µg/m <sup>3</sup>	Berwick et al. <sup>28</sup>
Cross-sectional 1 567 children aged 7 to 11 years	Palmes tubes for 2 weeks to estimate mean annual NO <sub>2</sub> household exposure	ATSQ given on three separate occasions for respiratory symptoms	15 ppb increase in NO <sub>2</sub> annual household mean associated with increased cumulative incidence of LRI	Neas et al. <sup>29</sup>
Cross-sectional 179 children aged 5 to 6 years	Passive diffusion monitors 0.005 to 0.161 ppm in bedrooms 0.009 to 0.292 ppm in living rooms	Questionnaire for respiratory symptoms and illness	No significant association found between average NO <sub>2</sub> levels and respiratory conditions	Meka et al. <sup>30</sup>
Case-control 231 aged 6	Palmes tubes and activity data 44 to 114 µg/m <sup>3</sup> 0.022 to 0.057 ppm	Questionnaire for symptom and illness occurrence	No difference occurred indoors between cases and controls	Hoek et al. <sup>31</sup>
Cross-sectional 362 children aged 7 to 13 years	Passive diffusion badges Levels 13.03 to 23.11 ppb	MRCQ and ATSQ used for illness and symptoms	No association between children's NO <sub>2</sub> exposure level and respiratory symptoms	Koo et al. <sup>32</sup>
Longitudinal and cross-sectional 1 051 children aged 6 to 12 years	Weekly Palmes tubes Average exposure 20 to 60 µg/m <sup>3</sup>	Modified WHOQ for respiratory symptoms	No association between NO <sub>2</sub> home exposure and reported respiratory symptoms	Dijkstra et al. <sup>33</sup>

### The Australian experience

The NSW State Pollution Control Commission (SPCC), in determining air quality guidelines for urban air pollutants, has adopted the National Health and Medical Research Council (NHMRC) maximum for NO<sub>2</sub> of 0.16ppm (1 hour maximum).<sup>36</sup> In 1988, the Commission reported that the ambient NO<sub>2</sub> level exceeded this one-hour goal on no more than seven days in that year in their monitored areas. This tends to indicate that outdoor NO<sub>2</sub> exposure is likely to be small and this is supported by the ambient studies reported previously (see Table 1).

In the same year, the first Australian study of indoor NO<sub>2</sub> levels was carried out in the Sydney metropolitan area and the adjacent Blue Mountains of New South Wales. NO<sub>2</sub> levels were measured in 46 homes using passive badge monitors. Up to 58 per cent of homes were found to exceed the NHMRC goal of 0.16 ppm.<sup>37</sup>

Ferrari and co-workers concluded that an estimated half a million residents are exposed to NO<sub>2</sub> levels that exceed the NHMRC goal to the extent of three hundred instances during a winter heating period. They suggest the number of instances would be much higher in the colder climates of Tasmania and Canberra.<sup>37</sup>

A recent discussion paper has reported on a study of the levels of NO<sub>2</sub> in over 600 New South Wales school classrooms resulting from the use of flueless gas heaters. The study was commissioned by the NSW Department of Education and co-ordinated by the SPCC with the assistance of the Australian Gas Light Company. Nitrogen dioxide levels ranged from 0.01 ppm to 2.90 ppm, being higher in poorly ventilated, unoccupied classrooms with greater heater use. However, even when directions were issued to schools to ensure adequate ventilation, 30 per cent of school rooms still had levels of NO<sub>2</sub> exceeding 0.16ppm.<sup>38</sup>

### Conclusions and recommendations

The World Health Organisation recommends maximum levels of 0.08 ppm over 24 hours and 0.21 ppm over one hour for ambient NO<sub>2</sub> exposure.<sup>6</sup> The NHMRC (recent recommendation) accepts that 'NO<sub>2</sub> may cause clinical effects in some individuals above 0.3 ppm hourly average'. The Australian experience would indicate that a significant number of people are exposed to more than 0.16 ppm of NO<sub>2</sub> hourly on average and that a large number may be exposed to more than 0.3 ppm of NO<sub>2</sub>, especially in school classrooms.

Serious doubts exist, for reasons already explained, about the interpretation of the previously reported studies which used ambient monitoring and gas cooking as surrogate measures of personal NO<sub>2</sub> exposure. Attempts have been made to determine personal exposure using indoor monitoring results and diaries of individuals' activities. Florey,<sup>19</sup> Berwick<sup>28</sup> and Melia<sup>30</sup> carried out home monitoring only, while Houthuijs<sup>23</sup> and Hoek<sup>31</sup> combined home monitoring with time activity data in an attempt to determine personal exposure. An attempt was made

to determine school indoor exposure in one study but monitoring was undertaken for one week only. This makes overall interpretation of these conflicting results difficult and does not provide adequate epidemiological evidence from which to set a maximum hourly or 24-hourly average indoor goal for NO<sub>2</sub>.

Epidemiological research is needed on Australian populations under local conditions. Respiratory responses of Australians to NO<sub>2</sub> exposure may differ from those of other countries and need to be defined. Study designs will need to incorporate strategies that allow accurate measurement of personal exposure, reliable prospective collection of respiratory illness data to overcome recall bias, and statistical techniques to determine the minimum NO<sub>2</sub> level which will cause illness.

Many schools in New South Wales rely on unflued gas heating in winter and provide an opportunity for cohort studies to be undertaken. Passive diffusion badge monitors allow time-controlled short-term monitoring to be developed and provide a means to measure hourly levels of NO<sub>2</sub> exposure in large numbers of children in classrooms. Combined with home monitoring, this would allow a determination of average 24-hourly and hourly personal exposure which would contribute significantly to data required by the NHMRC for setting of goals for maximum NO<sub>2</sub> levels. Collaboration with appropriate agencies and laboratories is vital to ensure accurate monitor preparation, exposure and analysis.

Daily respiratory diaries have been used effectively and efficiently by one of the authors as a means of data collection.<sup>39,40</sup> Properly designed, these diaries may be maintained either by parents or by children and allow prospective data collection to reduce the recall bias inherent in the large number of cross-sectional studies undertaken to date.

Such research is needed to determine if there is a health risk associated with exposure to low-level NO<sub>2</sub>. If there is no determined health risk, it would be unfair to impose arbitrary restrictions that may be financially detrimental to many organisations.

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**2023510491**

Antti-Poika, M., Nordman, H., Koskenvuo, M., Kaprio, J., and Jalava, M., "Role of Occupational Exposure to Airway Irritants in the Development of Asthma," Int Arch Occup Environ Health 64(3): 195-200, 1992.

The authors studied the potential role of occupational exposure in the etiology of asthma. Seventy-eight asthmatics and 56 non-asthmatics from the Finnish twin cohort were investigated by means of a postal questionnaire. The authors reported that "exposure to organic solvents was found only in the asthmatic members of the discordant pairs, and none of the nonasthmatic persons had been exposed to solvents." There were reportedly no statistically significant differences regarding exposure to other unspecific "irritants."

2023510492



## Role of occupational exposure to airway irritants in the development of asthma

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**Summary.** In order to study the role of occupational exposure in the etiology of asthma, 78 asthmatics and 56 nonasthmatics from the Finnish twin cohort were investigated by means of a postal questionnaire. Among those studied were 31 identical twin pairs discordant with regard to asthma (i.e., only one member of the pair had asthma). The questionnaire inquired into the diagnosis and status of the asthma, smoking habits, atopic background, smoking history of the parents, and history as regards pets, and requested a detailed description of occupational exposure to airway allergens and irritants. Classification into asthmatics and nonasthmatics was based on the information gathered with the questionnaire, supplemented by other information whenever possible. Estimation of exposure was based on the subject's own report, on the work descriptions, and on the general knowledge about the exposure levels associated with work tasks in question. Exposure to organic solvents was found only in the asthmatic members of the discordant pairs, and none of the nonasthmatic persons had been exposed to solvents. There were no statistically significant differences as regards exposure to other unspecific irritants. Combined exposure to organic allergens and airway irritants was more common in the asthmatics than in the nonasthmatics ( $P = 0.009$ ). Exposure to irritants was also more common among the asthmatics than the nonasthmatics with similar exposure to organic allergens ( $P = 0.004$ ).

**Key words:** Asthma – Occupational exposure – Twins – Airway allergens and irritants – Smoking

### Introduction

In a recent study on asthma in the nationwide Finnish twin cohort, the heritability of asthma was estimated to be only 35.6%. The majority of the pairs with asthmatic members were discordant with regard to asthma (i.e.,

only one member of the pair had asthma) [13]. This suggests that environmental factors play a major role in the etiology of asthma. Because the childhood environment of twins is similar, a possible explanation might lie in the different occupational exposure.

The underlying mechanism in occupational asthma induced by organic allergens such as flour and animal epithelia is an immunologic, mainly IgE-mediated reaction. In chemically induced occupational asthma, other unknown mechanisms are apparently involved as well. Chemicals identified as responsible for occupational asthma include stainless steel welding fumes [9], aluminum salts [18], organic acid anhydrides [12, 14], and diisocyanates [10].

The occupational environment may contain a multitude of chemicals, such as organic solvents, irritant gases, detergents, and welding fumes, which frequently give rise to respiratory complaints and are considered to irritate the airways unspecifically. It is not known whether long-term exposure to such substances plays a role in the etiology of clinical asthma. Hypothetically, occupational exposure to dusts and unspecific airway irritants might trigger asthma nonimmunologically or facilitate the penetration of allergens or hapten-forming chemicals by affecting the bronchial defense mechanisms [21].

The objectives of this study were to assess (1) whether the identical twins discordant with respect to asthma differed with respect to occupational exposure to airway allergens or irritants, (2) whether occupational exposure to unspecific airway irritants was more common among the asthmatics than among the nonasthmatics in the entire sample, and (3) whether combined exposure to both allergens and irritants was associated with asthma.

### Subjects and methods

**Subjects.** The Finnish twin cohort is a population-based sample of like-sexed adult twin pairs with 13888 twin pairs of which 4507 pairs are identical. The zygosity has been determined by a highly

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**Table 1.** Subjects of the study

	No.	Age (years)		Gender	
		Mean (SD)		Female	Male
<i>Pairs with both members participating</i>	48				
Concordant with respect to asthma	17	51	(13)	11	6
Discordant	31	51	(11)	15	16
<i>Pairs with only one member participating</i>	38				
Asthmatics	13	50	(15)	10	3
Nonasthmatics	25	44	(15)	11	14
<i>All subjects</i>	134				
Asthmatics	78	51	(12)	48	30
Nonasthmatics	56	48	(12)	26	30

**Table 2.** Criteria of atopy

Criterion	Asthmatics ( <i>n</i> = 46)	Non- asthmatics ( <i>n</i> = 17)
Both positive skin tests and prurigo	8 (17%)	1 (6%)
Positive skin tests	30 (65%)	6 (35%)
Prurigo in childhood	8 (17%)	10 (59%)

accurate questionnaire method validated by blood markers [17]. Questionnaires were sent to all pairs in 1975 (response rate 89%) and in 1981 (response rate 84%) [8].

The subjects of the present study comprised 106 pairs of identical twins of whom (1) both had responded to the questionnaires in 1975 or 1981 and at least one had reported having asthma diagnosed by a physician or (2) at least one had asthma as a hospital diagnosis in 1972-85 according to the national hospital discharge register. Sufficient data were gathered from 166 persons (78%).

Those persons who had had asthma before the age of 18 years were excluded from the study, whereafter the final material comprised 134 persons: 48 pairs and 38 twins with only one member of the pair participating in the study (Table 1).

**Criteria of asthma.** Classification into asthmatics and nonasthmatics was based on the questionnaire. Fifty-two persons reported having asthma diagnosed by a physician. The claim of having asthma could be checked from the hospital records of 22 cases, and no discrepancy was found between the hospital records and the subject's own report in these cases.

An additional 26 persons reported dyspnea triggered by general environmental irritants and/or allergens (such as grass pollen, animal epithelium, and cold). They were also classified as asthma cases.

**Criteria of atopy.** Classification as an atopic was based on (1) reported positive skin tests against several environmental allergens or (2) reported prurigo in childhood. Forty-six (59%) of the asthmatics and 17 (30%) of the nonasthmatics were classified as atopics (Table 2). Positive skin tests to environmental allergens were more often the classificatory criterion for the asthmatics than for the nonasthmatics. In addition, 42 of the atopics reported having rhinitis.

**Methods.** Data were collected by means of a postal questionnaire inquiring into the diagnosis and status of the asthma, smoking habits, atopic background, smoking history of the parents, and history as regards pets, and requesting a detailed description of occupational exposure to airway allergens and irritants. New questionnaires were sent to the nonrespondents after 2 weeks. Supplementary information was obtained by telephone interviews, when

**Table 3.** Occupations classified as involving exposure to a dusty environment

Agent	Occupation
Dusts in general	Farmer
	Construction worker
	Gardener
Peat dust	Foreman/tractor driver at a peat quarry
Asbestos	Insulator
Sand dust	Driver of a road scraper
Liquid wood impregnants	Industrial carpenter
Paper dust	Librarian
	Bookbinder
	Bookkeeper
	Bank clerk
	Post office clerk
Grease smoke	Baker
Leather dust	Leather worker
House dust	Hotel cleaner
Dacron dust	Inspector of Dacron textiles
Plastic chemicals	Process worker in the plastic industry
Stone dust	Worker in a stone-crushing plant
Tobacco smoke	Waiter
	Bar assistant

ever needed and possible (in 69 cases). The data on 60 cases were based on the telephone interview only.

The same physician asked questions about the asthma and exposure in the telephone interview. The information about asthma and exposure were, however, evaluated and coded by different persons independently of each other.

Three analyses were performed. First, a pairwise comparison was carried out in the pairs discordant with regard to asthma. Second, using a case-control design, occupational exposure was investigated with the whole material pooled. Third, in order to assess the possible association between asthma and combined exposure to allergens and irritants, a case-control design was used in a subgroup of the 50 persons occupationally exposed to major organic allergens (flour, animal epithelia, and molds). The asthmatics with such exposure (31) served as cases, and the nonasthmatics (19) as controls; exposure to irritants was compared between the cases and the controls.

**Estimation of exposure.** In the questionnaire, detailed descriptions of exposure to all occupational exposure agents were asked. 30 agents were specifically requested. The additional dusts and agents

which were spontaneously mentioned formed a group termed a "dusty environment." To avoid asymmetric reporting, the evaluation of exposure was not based on subjective reporting only; emphasis was placed on the work description and general knowledge about exposure in similar work tasks. All the farmers, construction workers, and gardeners were considered to be exposed to a dusty environment. The other occupations which were regarded as involving exposure to a dusty environment, independently of the subjects' own reports, are presented in Table 3.

The combined exposure to allergens and irritants consisted of exposure to the major organic allergens (flour, animal epithelia, and molds) and to airway irritants. The irritants present in these combinations were organic solvents, welding fumes, textile dust, formaldehyde, detergents, and irritant gases or dusts (asbestos and other insulation materials, construction and garden dusts, grease smoke, tobacco smoke, and paper, leather, peat, and stone dusts).

**Statistical methods.** In the comparison of the discordant twins, the McNemar test was used. The chi-square test for fourfold tables was used in the pooled material and Fisher's exact test was used when the smallest expected frequency was < 5.

**Table 4.** Atopy in the twin pairs discordant with respect to asthma (31 pairs).

	Asthmatic cotwin	
	Atopic	Nonatopic
Nonasthmatic cotwin:		
Atopic	8 (concordantly atopic)	1 (discordant for atopy)
Nonatopic	11 (discordant for atopy)	11 (concordantly nonatopic)

**Table 5.** Occupational exposure and smoking in the twin pairs ( $n = 31$ ) discordant with respect to asthma

	Number of pairs			McNemar test, <i>P</i> value
	Discordantly exposed		Concordantly exposed	
	Asthmatic member of the pair only	Nonasthmatic member of the pair only		
Smoking	6	0	4	0.014
Present smoker	4	0	1	0.045
Former smoker	2	0	3	>0.10
Occupationally exposed	9	5	18	>0.10
Organic solvents	4	0	0	0.045
Welding	4	1	0	>0.10
— of mild steel	4	1	0	>0.10
— of galvanized materials	2	0	0	>0.10
— of aluminum	1	0	0	>0.10
— of painted materials	2	1	0	>0.10
— of stainless steel	0	0	0	>0.10
Combination of organic allergens and irritants	5	2	1	>0.10
Pesticides	4	1	1	>0.10
Soldering flux fume	2	0	0	>0.10
Cutting fluids	2	0	0	>0.10
Irritant gases	2	0	2	>0.10
Flour	1	4	9	>0.10
Animal epithelium	0	3	10	>0.10
Molds	3	4	8	>0.10
Textile dust	1	3	2	>0.10
Dusty environment	4	5	4	>0.10

## Results

### Discordant twin pairs

Thirty-one out of 48 twin pairs were discordant with respect to asthma. Twelve of them were also discordant with respect to atopy (Table 4). In 11 pairs the asthmatic twin also displayed atopy, whereas in one pair, atopy was present in the nonasthmatic twin (McNemar test  $P = 0.004$ ).

Dissimilarity with respect to occupational exposure was found in 14 pairs: in nine pairs the asthmatic twin was exposed, in five the nonasthmatic (Table 5). As regards type of exposure agent, exposure to organic solvents was reported only by the asthmatic members of the pairs. Six pairs differed with regard to smoking habits: there were no pairs in which only the nonasthmatic twin had been a smoker.

### Occupational exposure among the asthmatics and the nonasthmatics in the pooled material

Sixty asthmatics (77%) and 40 nonasthmatics (71%) had been occupationally exposed to at least one agent. There was a difference between asthmatics and nonasthmatics concerning exposure to organic solvents (Table 6), to which none of the nonasthmatics had been exposed. In all instances, the solvent exposure had preceded the onset of asthma. Combined exposure to allergens and irritants was statistically significantly more common

**Table 6.** Exposure of the asthmatics and nonasthmatics (in the pooled material)

Exposure agent	Asthmatics (n = 78)		Nonasthmatics (n = 56)	
	No.	%	No.	%
Any exposure	60	77	40	71
Animal epithelium	22	28	17	30
Flour	28	36	17	30
Molds	25	32	18	32
Combined exposure to allergens and irritants	21	27*	5	9*
Textile dust	11	14	5	9
Wood dust	9	11	4	7
Organic solvents	8	10	0	0
Detergents	9	11	7	12
Welding fumes	7	9	3	5
Mild steel	6	8	3	5
Galvanized material	4	5	1	2
Aluminum	3	4	0	0
Stainless steel	3	4	1	2
Painted materials	4	5	2	4
Roots and vegetables	4	5	4	7
Formaldehyde	5	6	1	2
Cyanacrylates	2	3	2	4
Plastic degradation products	2	3	2	4
Dyes	2	3	2	4
Soldering flux fumes	2	3	0	0
Cutting fluids	2	3	2	4
Pesticides	6	8	5	9
Irritating gases	5	6	3	5
Metal dust (excluding chromium)	3	4	3	5
Dusty environment	43	55	30	54

\* Significant difference between asthmatics and nonasthmatics:  
 $P = 0.009$

among the asthmatics than the nonasthmatics. A similar, although not statistically significant, trend was found for exposure to flour, wood dust, textile dust, molds, and formaldehyde.

Only one asthmatic had been exposed to spices, isocyanates, or hairdressers' chemicals, and no person had been exposed to milk powder, enzymes, raw coffee, raw cotton, raw flax, epoxy compounds, pharmaceuticals, or photochemicals.

Smoking was less frequent among the asthmatics (18%) than among the nonasthmatics (37%) ( $P = 0.09$ ), whereas the asthmatics were more often ex-smokers (17%) than the nonasthmatics (9%) ( $P = 0.20$ ). Parental smoking was slightly more common among the asthmatics (62%) than among the nonasthmatics (50%) ( $P = 0.18$ ), but pets had slightly more often been present in the childhood of the nonasthmatics.

*Combined exposure to allergens and irritants  
(the case-control study in the subgroup  
exposed to organic allergens)*

Twenty-one (68%) of the asthmatics exposed to organic allergens had also been exposed to airway irritants,

whereas only five (26%) of the nonasthmatics had a similar combined exposure ( $P = 0.004$ ).

## Discussion

The hypothesis of the study was that occupational exposure would explain the discordance with regard to asthma in identical twins which had been discovered in an earlier study [13]. In the present study, 65% of the pairs were found to be discordant with regard to asthma, but no clear explanation for the discordance was found. Some of the results, however, suggest a role for both occupational exposure and smoking in the etiology of asthma.

Exposure to organic solvents was only found in the asthmatic members of the discordant pairs. In the pooled material, solvent exposure was also reported only by the asthmatics. There were no differences as regards exposure to other unspecific irritants, either in the pairwise analysis or in the pooled material. Combined exposure to allergens and irritants was clearly associated with asthma in the pooled material. Exposure to irritants was also more common in asthmatics than in nonasthmatics with similar exposure to organic allergens.

The proportion of discordance was clearly smaller (65%) in the present study than in the previous study on asthma in the same Finnish twin cohort [13], where 93% of the 148 identical pairs with asthma were discordant with regard to asthma. The discrepancy between the two studies is understandable, because the collection of cases and the criteria for asthma were different. In the earlier study, the cases were derived from the national hospital discharge register and the nationwide registry of the Social Insurance Institution for fully reimbursed medication. This means that the study was not dependent on the response of the subjects. It also means that subjects with milder disease were excluded from that study. Moreover, persons with childhood asthma, who were excluded from the present study, were included in the earlier study.

The precision of diagnosis is always problematic in questionnaire studies. The question presented was: "Have you been diagnosed as having asthma?" In addition, the place of diagnosis and details of the disease were requested. In a Swedish study [4], the consistency between questionnaire results and clinical diagnosis of asthma was fairly good; in only 2 of 39 cases did the diagnoses fail to correspond. We were able to check the hospital records in 22 cases without finding any discrepancy between the hospital diagnosis and the subject's report. Thus, we believe that the reliability of the answers is quite good.

It was more difficult to classify the 26 persons who reported that they had not been diagnosed as having asthma, but who cited symptoms which resembled asthma and which were triggered by general environmental allergens, irritants, or cold. Some of them even used asthma medication occasionally. For practical reasons, it was not possible to clinically verify the diagnoses, and the persons were classified as asthmatics if

the history given in the questionnaire suggested such a diagnosis. According to the nationwide registry for fully reimbursed medication [13], two of these persons were later provided with asthma medication free of charge, which means that their asthma had later been diagnosed by a physician and needed continuous medication.

In a case-control study, the reporting of exposure to unspecific irritants and a dusty environment is susceptible to a systematic error. Asthmatics, more often than healthy people, suffer from irritants and thus more readily report them. Therefore, stricter criteria were used in the evaluation of exposure. This probably diminished the effect of asymmetric reporting, a suggestion supported by the fact that the asthmatics no more frequently reported any exposure or exposure to a dusty environment than did the nonasthmatics. The stricter evaluation of exposure, however, probably misses some relevant information and thereby diminishes the sensitivity of the study.

Analyses 2 and 3 included data from individual members of twin pairs, i.e., the other member failed to respond. This could have caused systematic positive bias if the asthmatics had responded more often and reported exposure more actively than the nonasthmatics. Most of the respondents (66%) were nonasthmatics, however. The inclusion of the 13 "pairless" asthmatic members could cause a positive bias if their nonrespondent pairs were nonasthmatic and were occupationally exposed. Of these 13 asthmatics, one was exposed to solvents and three had combined exposure to organic allergens and irritants. If these 13 persons had been excluded from the analyses, the statistical significance would have diminished but not disappeared ( $P = 0.02$  in analysis 2 and  $0.01$  in the analysis 3). Thus, the bias, if there is any, is unlikely to explain the results totally.

The advantage of studying identical twins, with identical genetic sets and similarity of childhood background and living habits, may be evened out by the fact that, as it turned out, identical twins tend to choose similar occupations and thus to have similar working conditions. A tendency for asthmatics and atopics to work in "cleaner" occupations may also diminish the power of a study such as ours.

Our results are partly in concordance with those of earlier studies. Some chemicals are known to be capable of inducing bronchial hyperresponsiveness. Such chemicals include ozone [6], toluene diisocyanate [3], colophony, [2] sulfur dioxide [7], and tobacco smoke [5]. Our clinical experience suggests that organic solvents might trigger the onset of asthma but so far we have found no epidemiologic or experimental studies on the role of solvents in bronchial hyperresponsiveness. On the other hand, the association between combined exposure to allergens and irritants and asthma is in agreement with some recent studies which imply that exposure to irritants may injure the bronchial mucosa, facilitating the penetration of allergens, or by some other mechanisms increase the sensitization to allergens [1, 11, 15, 16, 19].

In the discordant pairs, only asthmatic twins were or had been smokers. Smoking was inversely related to asthma in the pooled material but the ex-smokers were

more common among the asthmatics. It is possible that asthma had led to giving up smoking, although this was not specifically investigated in the study. The role of smoking in allergy has been suggested by some epidemiologic and experimental studies [21]. Our results are consistent with the earlier study on the Finnish twin cohort [20], where smoking was not found to be a strong risk factor for asthma although the prevalence of asthma was slightly higher among male smokers.

Eleven of the pairs discordant with regard to asthma were discordant with respect to atopy as well. Thus atopic asthma may account for part of the discordance with respect to asthma, although the study did not offer any explanation for the 11 pairs being discordant with respect to atopy despite their identical genetical background and similar childhood conditions. The results must be evaluated with caution, however, because the determination of atopic cases was mainly based on skin tests, and it is obvious that asthmatic persons are skin tested more often.

The studied population was small and the number of persons exposed to individual agents was likewise small. Because there were also other factors diminishing the power of the study, conspicuous differences were hardly expected. Therefore, our results can be considered to support our hypothesis that long-term exposure to irritant substances (irritating substances in general and organic solvents in particular) may influence the development of clinical asthma of both allergic and nonallergic nature.

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The authors performed a population-based cohort study of 602 children aged 5-9 years to examine the possible effects of asthma on pulmonary function development in children. Spirometry was performed and a standardized respiratory and illness questionnaire was administered by trained interviewers every year for 13 years. The authors report that their results "demonstrate apparent sex differences in the relationship between asthma and lung function development, with males more likely to have asthma but females experiencing a greater deficit in pulmonary function. For example, females were at a greater risk of hospitalization for asthma than male asthmatic subjects.

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# Effects of Asthma on Pulmonary Function in Children

## A Longitudinal Population-based Study<sup>1-3</sup>

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### Introduction

To date only a few investigations (1-5) have explored the effect of a history of asthma on lung function in children. No study has characterized subjects at more than two points in time, and male-female differences have not been clearly explored. In this paper, we report on the analysis of data for a cohort of 602 children examined annually over a 13-yr period. During the course of the study, sufficient numbers of both male and female asthmatic children were identified to permit the characterization of male-female differences in the effect of asthma on pulmonary function.

Typically, asthmatic children have pulmonary function within the normal range in adolescence or young adulthood, with asthmatic symptoms tending to remit in a variable percentage as children grow (1-5). The presence of active symptoms is associated with lower levels of pulmonary function (1-4).

Cigarette smoking, direct (6) and passive (7, 8), has been shown to impair the growth of lung function in children and adolescents, and cross-sectional investigations have identified maternal smoking as a factor influencing airways responsiveness and level of lung function among asthmatic subjects (9, 10). Thus any analysis of lung function development among asthmatic subjects must take account of the effects of personal and maternal smoking. In our cohort, smoking history and other potential confounding factors have been documented through the use of a detailed annual questionnaire, and as a result, we are able to make appropriate adjustments to our estimate of the effect of asthma on pulmonary function.

### Methods

#### Population Selection and Screening

Details of the sample selection and screening have previously been reported (7, 11). Brief-

**SUMMARY** Data from a longitudinal study of childhood factors influencing the development of chronic obstructive lung disease were used to assess the effects of asthma on lung function development in male and female children. A population-based cohort of 602 white children, initially aged 5 to 9 yr, was observed prospectively for 13 yr. Spirometry was performed and a standardized respiratory and illness questionnaire was administered by trained interviewers on a yearly basis. Forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), and forced expiratory flow between 25 and 75% of vital capacity (FEF<sub>25-75</sub>) were used as measures of lung function. The total number of children reporting asthma over the course of the study was 67. Male asthmatic subjects (n = 42) had larger average percentage of predicted FVC than nonasthmatic males (n = 277). Female asthmatic subjects (n = 23) had a lower average percentage of predicted FEV<sub>1</sub> than nonasthmatic females (n = 280). In a multivariate analysis of the individual lung function measures, adjusting for previous level of pulmonary function, age, height, change in height, and personal and maternal smoking, males reporting active asthma had a significantly larger FVC than males with no history of asthma. In contrast, females with active asthma had a significantly smaller FEV<sub>1</sub> than females with no history of asthma. Both males and females with active asthma had decreased FEF<sub>25-75</sub>. From our analysis, we would predict that a female who develops asthma at age 7 would experience a 5% reduction in FEV<sub>1</sub> by age 10 and a 7% deficit by age 15. In our sample, asthmatic females had a greater risk of hospitalization for asthma than male asthmatic subjects (4 of 23, 6%, versus 1 of 42, 2%; p = 0.049). These results demonstrate apparent sex differences in the relationship between asthma and lung function development, with males more likely to have asthma but females experiencing a greater deficit in pulmonary function.

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ly, a 34% random sample was selected from all children aged 5 to 9 yr who enrolled in September 1974 in the public and parochial schools of East Boston, Massachusetts. East Boston is a small, geographically distinct, ethnically and socioeconomically homogeneous area of the city of Boston. All the children in our study are white and predominantly Italian-American.

These randomly selected 5 to 9 yr olds were considered the index children. Trained interviewers visited the households of the index children and enumerated all residents between January and June 1975. The residents of these households, including the index children, constituted the initial study population. Initial examination of the subjects was conducted between January and June 1975. Index subjects then were visited in their homes during the school year (September to June) for a total of 13 annual follow-up examinations. Other family members were visited in their homes only for follow-up examinations 3 through 13. Follow-up interviews were conducted whenever possible within 4 calendar weeks of the date of the previous year's interview, usually between 2:00 and 8:00 p.m. All follow-up examinations were performed by one of two original interviewers.

#### Respiratory Symptoms and Definition of Asthma

Standardized questionnaires were used to obtain a history of respiratory symptoms and illnesses, as well as smoking history and demographic data. At the initial examination and the first two follow-up examinations, sepa-

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rate questionnaires were used for subjects under 10 yr of age and for subjects 10 yr or older. A common questionnaire was used for all subjects in the third through thirteenth follow-up examinations. The questions relating to chronic respiratory symptoms were those proposed by the Division of Lung Diseases, National Heart Lung and Blood Institute for epidemiology studies (12, 13). For children aged 10 or younger, the parents answered all questions except those pertaining to the child's own smoking history; all other children answered all questions themselves.

Asthma was defined as an affirmative answer to the question, "Has a doctor ever told you that you (your child) have (has) asthma?" Any wheeze was defined as wheezing with colds or occasionally, apart from colds, or on most days and nights. For the purpose of the present analysis three different definitions of asthma were used. Subjects were defined as ever-asthma if they ever responded affirmatively to the question. All other subjects were defined as never-asthmatic. This definition disregarded disease activity and was used for the analyses presented in tables 2 and 3. In the longitudinal analyses, active asthma was considered present if a subject responded affirmatively to the ever-asthma question and had any wheezing symptoms in that study year. Subjects with a past history of asthma but who denied wheezing during the previous year were considered to have inactive asthma in that study year. This definition of active asthma was chosen because it has a high correlation with an objective test of airways responsiveness in a cross-sectional study of a representative sample of this population (14). An additional benefit of the active and inactive definitions is that the true natural history of the disease is being modeled (subjects can have active disease in one year, inactive disease the next and active disease the third, and these relationships are captured in the model).

Hospitalization and medication use were assessed by self-report of hospitalization or medication use in each survey year. Respiratory illness before age 2 was defined as parental report of a doctor's diagnosis of pneumonia, bronchitis, croup, or bronchiolitis before age 2.

#### Definitions of Cigarette Smoking

A mother was considered a current smoker if she had been smoking within 1 month before the time of interview for the initial examination or for the entire year before and including the time of interview for the follow-up examinations. Exsmokers were defined as those who had smoked more than 20 packs in their lifetime or more than one cigarette per day but had stopped smoking more than 1 month before the interview. For the purpose of the analysis, children with never and exsmoking mothers were compared with children with currently smoking mothers.

The child's smoking history was obtained directly from all children during pulmonary function testing, a time when parents were

not present. A child was considered a current smoker if he or she smoked at least one cigarette per day within 1 month of the interview. For the purposes of this analysis, never-smokers and exsmokers were compared with current smokers.

#### Spirometry

Forced vital capacity (FVC) maneuvers were performed with the subjects seated without nose clips using an 8-L, water-filled portable spirometer (Survey spirometer; Warren E. Collins, Inc., Braintree, MA). Tests were performed by one of two of the same technicians (one technician performed > 90% of the tests) throughout the entire study. A test was considered acceptable if the technician assessed that a maximum effort had occurred in the face of no other technical problems (e.g., mouth leak) and all criteria for an acceptable timed forced expiratory volume (12) were met. Subjects aged 10 yr or less were encouraged to blow for at least 4 s and those over 10 yr were encouraged to blow for at least 6 s. Five acceptable tracings with vital capacities within 5% of the maximum were sought; up to eight attempts were permitted.

All tracings were hand measured by the same technician for the first nine surveys and by a second technician for the last four surveys. The second technician was standardized to the first technician on a regular basis to assure the comparability of the measurements across surveys. All volumes were corrected to body temperature and pressure saturated with water vapor (BTPS). Three measures of pulmonary function were obtained from the spiograms: FVC, forced expiratory volume in one second (FEV<sub>1</sub>), and forced expiratory flow between 25 and 75% of the vital capacity (FEF<sub>25-75</sub>). FEV<sub>1</sub> measurements with appropriate back extrapolation were accepted from tracings from which FVC measurements could not be made (12). In the present analysis, the maximum recorded FEV<sub>1</sub>, FEF<sub>25-75</sub>, and FVC (13) (not necessarily from the same tracing) were used. Each subject's standing height (ht) without shoes was measured to the nearest 0.5 inch and converted to centimeters for this analysis. Mean function values were converted into percentage of predicted values using the nomograms of Dickman and colleagues (15).

#### Methods of Data Analysis

For preliminary percentage of predicted analyses (table 2), pulmonary function was compared by two-sample *t* tests with two-sided *p* values. Two-sample *t* tests with two-sided *p* values were used to compare, by sex, asthmatic subjects with respect to age of onset of asthma, total number of years of active asthma, total number of years of medication for asthma, number of years smoking, and total number of cigarettes smoked. Fisher's exact test with two-sided *p* values calculated according to the "horizontal line method" (16) was used to compare the numbers of male and female asthmatic subjects reporting hos-

pitalization for asthma and illness before age 2, and by sex the numbers of asthmatic and nonasthmatic personal ever-smokers.

A first-order autoregressive model (8, 17) was used to estimate the effect of smoking and asthma history on lung function separately for males and females. This method accommodates the longitudinal nature of the data and is particularly easy to implement and interpret because it is implemented using a modification of linear regression, a technique included in most statistical software packages. The usual linear regression model is not appropriate for longitudinal data because the repeated observations on individuals are not independent.

To implement the method the natural logarithm of lung function at each time period for each child was used as the dependent variable in a linear regression that included lung function in the previous time period as an independent variable along with sex, age, height, change in height, maternal smoking, personal smoking, active asthma, and inactive asthma. Adjustment for the residual correlation between the lung functions of siblings in the same study year was accomplished by including a random effect for each family study-year combination (18). The differential effects of sex were examined by including interaction terms between sex and the independent variables. Sex, the asthma variables, and the sex-asthma interactions were kept in all models, but other sex interaction terms were retained only if they were statistically significant. Model adequacy and validity were checked by examining residual plots and autocorrelation functions (19).

Finally, a second-order autoregressive model was fit to the data, and these results compared to the results of the first-order autoregressive model. This model predicts the current pulmonary function as a function of the two previous years values. Because this model reduces the effective sample size by 25% and thus adversely effects study power and because, in our judgment, the results were essentially the same as the first-order models, only the first-order results are presented in table 4. We note that the second-order term was significant for each of the three lung function measures, however, thus indicating the possibility of an improved fit using second-order models. The results of the first- and second-order models are contrasted in table 5.

The coefficient for the current asthma variable can be interpreted as the increase or decrease in the logarithm of lung function in any given time period associated with the presence of current asthma, holding constant all other terms in the model, including lung function in the previous period. A method for propagating the increase or decrease over several periods is given by Rosner and coworkers (17) and has been modified slightly to produce the projections shown in figures 1 and 2. Because our regression model used the logarithm of lung function, we obtained the percentage effects shown in table 4 by exponentiating the appropriate regression

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coefficients, subtracting 1, and multiplying the result by 100.

For the models shown in table 4, we estimated residual correlations between the logarithms of lung functions for siblings seen in the same year as 0.35 for FVC, 0.25 for FEV<sub>1</sub>, and 0.19 for FEF<sub>25-75</sub>. Although these correlations are significant and were taken into account in the final models, we found the effect of ignoring the familial clustering to be minor on the estimates of other model parameters.

### Results

A total of 602 subjects initially between 5 and 9 yr of age contributed data to the analysis over the 13-yr period. These 602 subjects included 346 index subjects and 256 siblings from 334 families. An additional 193 children in this age range were initially seen in Year 1 but contributed no data to the analyses. They represented siblings of the index subjects who were not seen in Years 2 and 3 of follow-up and a small number of index subjects with missing data. The included and excluded subjects are compared with respect to their baseline characteristics in table 1. No significant differences are apparent. Included subjects were on average 6.9 yr of age at study onset, were overwhelmingly nonsmokers, and had normal pulmonary function in the initial survey.

At baseline male active asthmatic subjects had a significantly lower FEF<sub>25-75</sub> than male nonasthmatic subjects, and female active asthmatic subjects had a significantly lower FEV<sub>1</sub>, compared to female nonasthmatic subjects (table 2). A preliminary analysis was performed to examine the average percentage of predicted pulmonary function at baseline and over the 13-yr period for asthmatic and nonasthmatic subjects stratified by gender (table 2). When compared with nonasthmatic males, ever-asthmatic males had a 3% higher FVC, a 3% lower FEV<sub>1</sub>, and an 11% lower FEF<sub>25-75</sub>. Ever-asthmatic females when compared to nonasthmatic females, however, had no difference in average percentage of predicted FVC but a 9% reduction in percentage of predicted FEV<sub>1</sub>, and an 18% decrease in percentage of predicted FEF<sub>25-75</sub>.

Male and female ever-asthmatic subjects were similar with regard to a number of clinical characteristics (table 3). Females, however, were significantly more likely than males to have been hospitalized for asthma.

Male ever-asthmatic subjects did not differ from nonasthmatic males in the percentage of personal ever-smokers (5

of 42, 12%, versus 23 of 277, 8%;  $p = 0.556$ ), lifetime number of cigarettes smoked (3.45 versus 3.45 pack-years;  $p = \text{NS}$ , not significant), or average number of years smoking (2.98 versus 2.91,  $p = 0.794$ ). The data for females are suggestive of a difference between ever-asthmatic and nonasthmatic subjects in the

percentage of personal ever-smokers (9 of 23, 39%, versus 54 of 260, 21%;  $p = 0.063$ ) and the average lifetime number of years smoking (2.35 versus 2.98,  $p = 0.062$ ) but not in the average number of cigarettes smoked (3.20 versus 3.46 pack-years;  $p = 0.555$ ).

To evaluate the effect of the time-

TABLE 1  
COMPARABILITY OF SUBJECTS INCLUDED AND EXCLUDED FROM  
ANALYSIS FOR SELECTED CHARACTERISTICS  
IN THE ENTRY YEAR

	Included	Excluded	p Value*
Numbers	602	193	—
Age (x ± SD), yr	6.9 ± 1.3	7.0 ± 1.3	0.407
Height, (x ± SD), cm	122.4 ± 9.4	121.9 ± 10.4	0.646
FEV <sub>1</sub> , (x ± SD), L	1.15 ± 0.19	1.14 ± 0.21	0.571
Asthma, wheeze, n (%)†	30 (5.2)	11 (6.0)	0.327
Mother's smoking, n (%)‡	191 (26.9)	57 (33.5)	0.532
Sex, male, n (%)	303 (52.5)	99 (51.3)	0.411
Personal smoking, nonsmokers, n (%)§	523 (97.8)	135 (98.5)	0.798

\* Two-sided p value for two-sample t tests or chi-squared tests

† Two asthmatic subjects missing Year 1 data

‡ There were 75 mothers missing smoking information in Year 1, 52 not in the model for males and 23 not in the model for females

§ There were 98 children missing personal smoking information in Year 1, 42 from the included group and 56 from the excluded group

TABLE 2  
AVERAGE PERCENTAGE PREDICTED VALUES FOR PULMONARY FUNCTION  
AT ENTRY AND OVER 13 YR OF OBSERVATION FOR ASTHMATIC  
AND NONASTHMATIC SUBJECTS BY SEX

	FVC		FEV <sub>1</sub>		FEF <sub>25-75</sub>	
	Mean ± SD	p Value	Mean ± SD	p Value	Mean ± SD	p Value
Males						
At entry						
No asthma	101 ± 15	0.734	105 ± 16	0.675	88 ± 20	0.037
Active asthma	102 ± 18		103 ± 22		76 ± 25	
13-yr average						
No asthma	100 ± 12	0.130	103 ± 12	0.267	92 ± 18	0.003
Ever asthma	103 ± 11		100 ± 13		80 ± 22	
Females						
At entry						
No asthma	108 ± 14	0.529	116 ± 16	0.038	95 ± 21	0.072
Active asthma	104 ± 17		102 ± 16		73 ± 30	
13-yr average						
No asthma	110 ± 13	0.536	113 ± 12	0.012	100 ± 19	0.003
Ever asthma	106 ± 13		104 ± 16		82 ± 26	

\* p Value for difference

TABLE 3  
CHARACTERISTICS OF ASTHMATIC SUBJECTS  
INCLUDED IN THE ANALYSES

	Male, n = 42		Female, n = 23		p Value
	Mean	SD	Mean	SD	
Age asthma began	7.29 ± 4.66		8.61 ± 5.39		0.327
Years of asthma symptoms	3.07 ± 2.31		3.22 ± 2.02		0.793
Years of asthma medication	1.67 ± 1.99		2.26 ± 2.14		0.279
Illness before age 2*	14/42 (33%)		7/22 (32%)		0.762
Ever hospitalized for asthma	1/42 (2%)		4/23 (6%)		0.049†

\* One subject missing information on illness before age 2

† By Fisher's exact test

dependent variables, active and inactive asthma, with appropriate adjustment for the longitudinal structure of the data, including baseline differences in lung function, a first-order autoregressive model was used. Adjustment for height and growth velocity were accomplished by including height and change in height at each visit as independent variables in the regression model. Interaction terms between sex and active and inactive asthma were used to assess sex-specific effects. A random-effects approach was used to adjust for the residual correlation among siblings included in the same analysis.

The final models for all three lung function measures included previous lung function, sex, height, change in height, age, and maternal and personal smoking as independent variables. For FEV<sub>1</sub> and FVC, sex-height and sex-age interactions were included because preliminary fits of the model showed those interactions to be statistically significant. Maternal smoking was included for FEV<sub>1</sub> and FEF<sub>25-75</sub>. A sex-growth interaction was included in the final model for FEF<sub>25-75</sub>, and a sex-previous lung function interaction was included for FVC.

The sex-specific effects of active and inactive asthma, expressed as a percentage of the expected change in pulmonary function/year under the autoregressive model for children without asthma, holding growth and pulmonary function in the preceding year constant, are shown in table 4. The effect of active asthma on FVC was positive and statistically significant for males after adjustment for all other covariates in the model. Active asthma was not a significant predictor of change in FEV<sub>1</sub> for males. In contrast, for females the effect of active asthma was negative and statistically significant for change in FEV<sub>1</sub>, but not for change in FVC. For change in FEF<sub>25-75</sub>, the effect of active asthma was negative and statistically significant for both males and females. Inactive asthma was not a significant predictor for change in any measure of pulmonary function for either gender. The male-female difference column of table 4 provides a p value for the statistical significance of the difference between the effects of asthma in males and females. Overall, the findings from the autoregressive models confirm the pattern observed in the preliminary Percentage of predicted analyses.

Substantial agreement is seen between the first- and second-order autoregressive models for the effect of active asthma

TABLE 4  
SEX-SPECIFIC EFFECTS OF ASTHMA ON CHANGE IN PULMONARY FUNCTION (FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub>) AS ESTIMATED FROM AUTOREGRESSIVE MODELS\*

	Male		Female		Male-Female	
	Effect (%)	p Value	Effect (%)	p Value	Difference	p Value
FVC						
Active asthma	2.45	0.002	-0.76	0.451	3.21	0.012
Inactive asthma	0.70	0.308	-1.05	0.437	1.75	0.246
FEV <sub>1</sub>						
Active asthma	0.10	0.896	-2.12	0.034	2.22	0.077
Inactive asthma	0.13	0.846	-1.87	0.177	2.00	0.191
FEF <sub>25-75</sub>						
Active asthma	-4.18	0.003	-5.75	0.002	1.57	0.482
Inactive asthma	-0.54	0.666	-2.88	0.255	2.34	0.669

\* See text for variables included in the models. The mean effect of asthma (active and inactive) expressed as a percentage of the expected in pulmonary function for children without asthma, holding constant growth and pulmonary function in the preceding year. Refer to the text and figures 1 and 2 for assessing the cumulative effects over several years.

TABLE 5  
COMPARISON OF ESTIMATES FOR THE EFFECT OF ACTIVE ASTHMA FROM FIRST- AND SECOND-ORDER AUTOREGRESSIVE MODELS

Pulmonary Function	Model	Males		Females	
		Estimate (% effect)	p Value	Estimate (% effect)	p Value
FVC	First order	2.45	0.002	-0.76	0.451
	Second order	2.68	0.001	-0.55	0.618
FEV <sub>1</sub>	First order	0.10	0.896	-2.12	0.034
	Second order	0.55	0.497	-1.73	0.109
FEF <sub>25-75</sub>	First order	-4.18	0.003	-5.75	0.002
	Second order	-2.29	0.109	-2.78	0.150

ma (table 5). Examples of the sex-specific effects of asthma on lung function development implied by the final models for FVC and FEV<sub>1</sub> are provided graphically in figures 1 and 2. Each figure shows the projected mean pulmonary function for ages 8 through 15 for children of the same sex who begin at age 7 with the same initial level of lung function and height and experience the same growth in height at subsequent ages. The initial height and lung functions are taken from the medians in the population, as are the heights at each age. Projections for FVC are shown in figure 1, and projections for FEV<sub>1</sub> are shown in figure 2. From the data used to generate figure 2, we calculate that a female with a continuing history of asthma achieves only 95% of the FEV<sub>1</sub> by age 15.

It is important to note that age of onset of asthma is implicitly included in the autoregressive model. This is because effects persist over time in the model, with the result that older ages of onset result in smaller net effects on lung function at later ages.

## Discussion

Because of the potential importance of maximally attained level of FEV<sub>1</sub> as an indicator of future risk of chronic obstructive lung disease (20), the most important finding of this investigation is a deficit in change in FEV<sub>1</sub> for girls with a doctor's diagnosis of asthma and active wheezing symptoms. This deficit was less significant in female subjects with a past diagnosis of asthma but no active wheeze symptoms. The link between active asthma and lung function is less clear in male children. Males with active asthma had a greater change in forced vital capacity. However, both males and females with active asthma had a reduced change in FEF<sub>25-75</sub>. It should be stressed that these children are a random population sample of the East Boston community. The initially normal level of pulmonary function (table 3) is consistent with this. However, the observed effect should not be construed as not clinically or biologically significant. The deficit in growth in these mildly asthmatic subjects would place the FVC and FEF<sub>25-75</sub> results

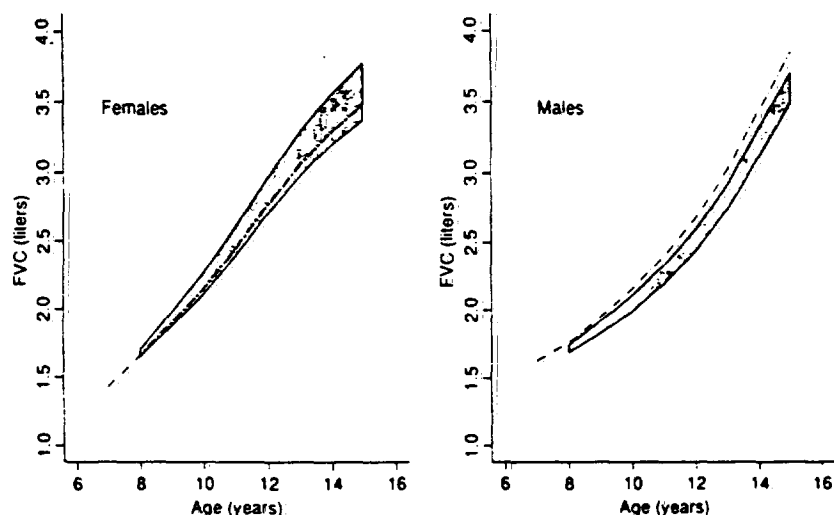


Fig. 1. Projected FVC for female and male subjects from age 8 to age 15. The shaded area represents confidence limits for the projected FVC of normal subjects. The broken line is the projected FVC for subjects with active asthma beginning at age 7.

for males and the FEV<sub>1</sub> and FEF<sub>25-75</sub> results for females outside the 95% confidence limits for normal change in growth of lung function in this random population sample.

Few longitudinal studies of the effect of asthma on lung growth exist. The largest prospective study of the effect of asthma on lung growth in children was performed by Williams and McNicol in Australia (1-4, 21). A total of 378 asthmatic and 105 control subjects were initially seen in 1964, again in 1967, and in 1981, 14 yr later; 331 (88%) of the asthmatic and 72 (69%) of the control subjects were seen in the second follow-up. Subjects with current symptoms were

likely to have reduced levels of both FEV<sub>1</sub> and FEF<sub>25-75</sub>. Martin and colleagues, analyzing a subgroup of this cohort, reported that those subjects with asthma that persisted from childhood were more likely to have both an elevated vital capacity and total lung capacity than those with intermittent symptoms (2). They also noted that girls did less well during adolescence than boys such that the gender ratio for severe disease was equal (4). Thus, their results are consistent with our observations.

The crude analysis comparing average percentage of predicted lung function in ever-asthmatic subjects (table 2) provides, for the most part, slightly larger

values for the differences between groups than the longitudinal modeling analyses, which consider active and inactive asthma (table 4). This may be because the longitudinal modeling explicitly controls for baseline or initial lung function and growth, whereas the crude analysis does not. The congruence between the crude and the multivariate modeling confirms that these results are not an artefact of the modeling process.

Asthma is more prevalent in boys than girls in both our cohort and the U.S. population (22). Lack of sex stratification, as in the study of Martin (2), would result in a balancing out of the male-female differences weighted toward the male (more prevalent effect). This tends to confirm the common clinical dictum from early investigators that childhood asthma has a relatively benign effect on lung function, particularly in boys (23). Our results for females suggest that this is not the case. The estimated deficit in FEV<sub>1</sub> for a female child with active asthma for 8 yr beginning at age 7 is 7%. This effect is substantially greater than the effect of passive smoking previously observed in this cohort (8) and places this female child below the 95% confidence limits for normal growth in this population. This degree of decrement in FEV<sub>1</sub> may have important implications for the development of chronic lung disease in adulthood. The finding that active wheeze symptoms (active asthma, table 4) were necessary for female asthmatic subjects to experience a reduction in lung function is consistent with the concept that active airway inflammation is responsible for the reduced level of pulmonary function and provides a useful clinical marker for disease severity to assist clinicians.

In addition to reduced change in FEV<sub>1</sub> and FEF<sub>25-75</sub>, female asthmatic subjects were more frequently hospitalized than the males (table 3). The association of hospitalization with asthma in female children is all the more striking given that, in this and other population studies of children, asthma was more common in males (24, 25). This formulation is also consistent with epidemiologic data from other population-based studies suggesting more severe asthma in female adults (25-27).

Mead used the term "dysanapsis" to indicate nonisotropic (nonproportionately equal) growth of airways and lung parenchyma resulting in either a lung that is too large or airways that are too small, or both (28). To the extent that the FEF<sub>25-75</sub> reflects airways size and the FVC represents lung size, our data sup-

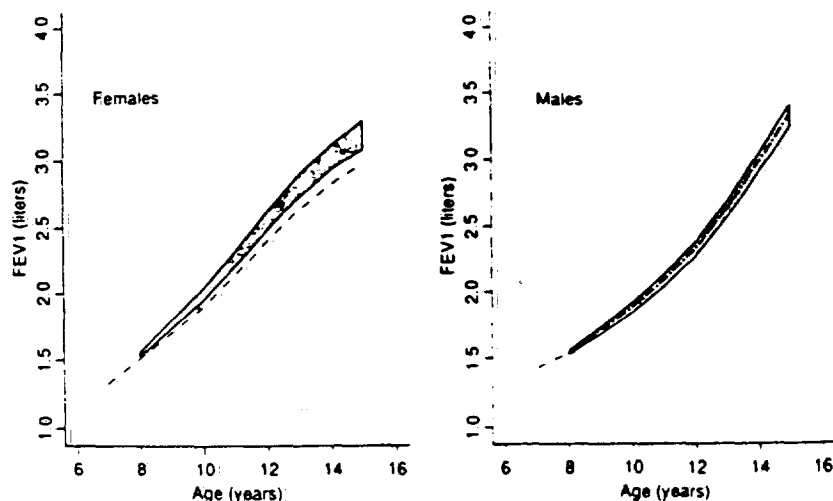


Fig. 2. Projected FEV<sub>1</sub> for female and male subjects from age 8 to age 15. The shaded area represents confidence limits for the projected FEV<sub>1</sub> of normal subjects. The broken line is the projected FEV<sub>1</sub> for subjects with active asthma beginning at age 7.

port the hypothesis that dysanapsis characterizes children with asthma. In a prior investigation of 291 children from this cohort with eucapnic hyperpnea using subfreezing air as a test of bronchial responsiveness, we demonstrated that children with a decreased  $FEV_{25-75}/FVC$  ratio were more likely to respond to bronchial challenge (29). In asthmatic males, dysanapsis may be attributable in part to an increased FVC. Thus, our results are consistent with the hypothesis that mechanical factors (e.g., dysanapsis) rather than simply airway inflammation are important in determining lung function in asthmatic males. Thus as lungs and airways grow, wheezing on a mechanical basis (dysanapsis) may be less common. The relationship between dysanapsis and airway responsiveness is unclear, however, and requires further investigation.

Greaves and Colebatch (30) suggested a complementary hypothesis based on a study of 18 asthmatic subjects. Of the subjects 10 developed asthma in childhood (all were males) and 8 developed asthma after age 18 (5 males and 3 females). The male childhood asthmatic subjects had an increased total lung capacity (TLC); adult-onset asthmatic subjects had a normal TLC. Analysis of pressure-volume curves revealed the male childhood asthmatic patients to have lungs of greater distensibility but adult-onset asthmatic patients had lungs of normal distensibility. Under their hypothesis episodes of bronchospasm postnatally could influence the growth patterns in childhood asthma. This hypothesis also requires further evaluation.

Certain aspects of our study design and population must be noted. First, subjects initially were aged 5 to 9 at study onset and over half of our asthma subjects were diagnosed before study onset. As Martinez and coworkers noted, however, abnormal lung function may antedate and predict subjects at risk of wheezing symptoms (31). Without information on the pulmonary function of the cohort from birth, it is difficult to be conclusive about whether our observed differences in patterns of lung growth for both male and female asthmatic subjects are cause or consequence of a diagnosis of asthma, or both. Although male subjects with active asthma at entry had significantly lower  $FEV_{25-75}$  and female subjects with active asthma at entry had significantly lower FEV<sub>1</sub> (table 2), initial lung function was controlled for in our regression analysis and thus differences in this factor are unlikely to explain our results.

the longitudinal results of Sherrill and coworkers (32). Despite the limitations in causal interpretation, the quantitative nature of our results and the described patterns of change in pulmonary function are of value to clinicians and investigators interested in asthma.

It is unlikely that maternal and personal smoking account for the different effects of asthma on change in lung function in males and females observed in our study. Males and females with asthma did not differ in percentage of smoking mothers from children without asthma. Asthmatic children were more likely to report personally ever smoking than children without asthma, but significantly so only for females. In addition, the effect of these variables was adjusted for in the analysis. Finally, male and female asthmatic subjects did not differ from their nonasthmatic same-sex counterparts in terms of amount and duration of personal cigarette smoking.

A self-report of a doctor's diagnosis of asthma is a standard definition for asthma used in respiratory epidemiology in the United States. It is based on a standardized questionnaire (33). This definition has been used by the National Center for Health Statistics and other government agencies in surveys of the U.S. population. Indeed, our asthma prevalence figures are comparable to national data (12). Thus, our definition is standard in epidemiology and is generalizable to other U.S. populations.

Diagnostic bias inherent in a doctor's diagnosis of asthma is less of a problem in children than in adults (34). However, it is important to consider misclassification of disease on our results. There is a large body of data in both our own (11, 14) and other populations (35, 36) that suggests that physicians tend to underdiagnose asthma. To the extent that this occurred in our study, the estimates of the effect of asthma on lung function are likely to be conservative.

Current concepts of asthma as a disease incorporate the notion of bronchial hyperresponsiveness (37). As alluded to in Methods, we performed a cross-sectional study to examine the prevalence of bronchial hyperresponsiveness to cold air in a random subsample of this cohort (14). In addition, results similar to those presented here were obtained when we examined airway responsiveness in this population (38). In this investigation, 11 of 12 asthmatic subjects with any wheezing in the current study year had increased bronchial responsiveness using a cutoff value for cold air challenge of a

FEV<sub>1</sub>/FVC. The one active asthmatic subject who did not meet this definition had a borderline (8%) decrease. No inactive asthmatic subjects had a positive cold air challenge test (14). These data tend to give credibility to our definition of asthma and to link a report of active asthma in this investigation with increased levels of bronchial responsiveness.

Simple differences in the prevalence of airway responsiveness and allergy (as manifested by skin test reactivity) also cannot explain our results. Increased airway responsiveness in populations tends to parallel the prevalence of asthma and hence is more common in males, especially at younger ages (39, 40). In children and young adults (aged 5 to 24) in our population, the prevalence of increased airway responsiveness was similar in males and females (14). Males in this and other populations are more likely to manifest allergy as measured by skin test reactivity (22, 26, 41). It is also unlikely that ethnic or socioeconomic differences between children in this cohort can explain our results, since the cohort is all white, predominantly Italian, and socioeconomically homogeneous. In addition, subjects come from a geographically defined area of the city of Boston, making differential effects of other factors, such as air pollution, unlikely. A number of other variables differ between males and females, such as height, change in height (growth), and muscle strength. Although these factors may be expected to contribute to the observed effects, height and growth were both accounted for in the analysis.

Prior analyses in this population demonstrated the importance of acute lower respiratory illness (LRI) as a predictor of the occurrence of asthma (41, 42) and as a predictor of reduced level of FEV<sub>1</sub> and FEV<sub>25-75</sub> and of longitudinal change in FEV<sub>1</sub> and FEV<sub>25-75</sub> (43). We directly assessed the role of retrospectively collected respiratory illness data using the illness before age 2 variable and found that this variable was not a significant predictor of longitudinal change in pulmonary function after inclusion of asthma in the model. These results are consistent with the results of Gold and coworkers (43). Whether these results are a function of recall bias, a strong causal relationship between LRI and asthma as suggested by Sherman and colleagues (42), or other factors is unclear. The role of prospectively collected LRI data on asthma and lung function has been reported previously (43). However, definitive assessment of the relationship

tion requires prospectively collected data from birth to age 5 yr, a time period that antedates the age of entry to this investigation. Our analysis leaves unanswered the mechanism by which asthma exerts these effects. It is hoped that ongoing longitudinal studies will address these issues more completely.

It is important to consider the impact of treatment on our results. On average, males and females did not differ in their duration of asthma treatment (table 3) but the duration of treatment was substantially less than the duration of asthma symptoms (table 3). When treatment was included in the regression model, it was not a significant predictor for any of the indices of pulmonary function and asthma remained significant (results not shown). Nevertheless, these data do not directly address the important question of whether aggressive, sustained treatment of asthma in childhood can influence the observed effects of asthma on lung function in children.

In summary, this longitudinal analysis demonstrates male-female differences in the influence of asthma on change in lung function as represented by FVC, FEV<sub>1</sub>, and FEF<sub>25-75</sub>. Asthma was more prevalent in males but more severe as measured by level of function and hospitalization in females in this cohort. Even in mild asthma with initially normal pulmonary function, the growth patterns lie outside the 95% confidence limits of nonasthmatic children. Whether the effects of asthma on change in pulmonary function observed in this study are linked to the airway abnormalities or are linked in some more fundamental way to hormonal, nutritional, or other influences on lung growth and maturation is unknown and unanswerable from the present analysis. Further research is necessary to determine the reasons for these differences and their implications for adult lung disease.

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Martinez, F.D., Wright, A.L., Holberg, C.J., Morgan, W.J., and Taussig, L.M., "Maternal Age as a Risk Factor for Wheezing Lower Respiratory Illnesses in the First Year of Life," American Journal of Epidemiology 136(10): 1258-1268, 1992.

The authors of this study examined the incidence of lower respiratory tract illnesses during the first year of life in 1200 infants in Tucson, Arizona. The authors reported that the incidence of wheezing LRIs increased significantly with decreasing maternal age, whereas the incidence of nonwheezing LRIs was independent of maternal age. Infants whose mothers were less than age 21 years had an odds ratio of 2.4 (95% CI: 1.8-3.1) compared with infants whose mothers were over 30 years of age. Infants whose mothers were aged 21-25 had an odds ratio of 1.8 (95% CI: 1.4-2.3) and infants whose mothers were 26-30 had a risk of 1.4 (95% CI: 1.1-1.6). The authors conclude that "these results suggest that young motherhood is an important risk factor for wheezing lower respiratory tract illnesses during the first year of life."



## Maternal Age as a Risk Factor for Wheezing Lower Respiratory Illnesses in the First Year of Life

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Postneonatal mortality due to respiratory illnesses is known to be inversely related to maternal age, but the possible role of young motherhood as a risk factor for respiratory morbidity in infants has not been thoroughly explored. The authors studied the incidence of lower respiratory tract illnesses during the first year of life, as ascertained by health plan pediatricians, in over 1,200 infants enrolled at birth between 1980 and 1984 in Tucson, Arizona. The incidence of wheezing lower respiratory tract illnesses increased significantly ( $p = 0.005$ ) with decreasing maternal age, whereas the incidence of nonwheezing lower respiratory tract illness was independent of maternal age. A logistic regression was used to control for the effects of several known confounding factors. When compared with infants of mothers aged more than 30 years, adjusted odds ratios were 2.4 (95% confidence interval 1.8–3.1) for infants whose mothers were less than age 21 years ( $p < 0.0001$ ), 1.8 (95% confidence interval 1.4–2.3) for infants whose mothers were aged 21–25 ( $p < 0.0001$ ), and 1.4 (95% confidence interval 1.1–1.6) for infants whose mothers were aged 26–30 ( $p < 0.001$ ). These results suggest that young motherhood is an important risk factor for wheezing lower respiratory tract illnesses during the first year of life. Both biological and social factors related to maternal age may explain these findings. *Am J Epidemiol* 1992;136:1258–68.

bronchiolitis; maternal age; men; women

In 1959, Morrison et al. (1) reported that postneonatal mortality for "respiratory diseases" and "accidents" (the latter including most cases of sudden, unexpected death) was highest among children of mothers aged less than 20 years and lowest among those of mothers age 30 or more. These trends associated with maternal age were particularly

noticeable for deaths occurring between 4 weeks and 6 months of age and were independent of birth rank, social class, and region of the country where the family lived (1). No such trends were observed for deaths due to "congenital malformations." The authors suggested that younger mothers may take less care during pregnancy and may provide poorer care for their infants in the postnatal period. They speculated that real biological factors related to maternal age may also affect the infant's capacity to meet environmental stresses.

Since that study was published, the possible association of maternal age with infant mortality has been a subject of considerable scrutiny. A recent report by Friede et al. (2), based on over two million births, confirmed a significant inverse relation between maternal age (up to age 29 years) and postneonatal mortality, independent of birth weight and

race. The causes of infant mortality in young infants of younger mothers have not been fully elucidated. Some studies have shown a role of biological factors affecting fetal development (3), whereas others have shown that poor parenting skills and lack of prenatal care may explain the reported findings.

A better understanding of these factors may enhance postneonatal survival in younger mothers. The relation between maternal age and neonatal morbidity and mortality in such studies are often difficult to interpret, attributable to the lack of well-controlled studies in infancy. Studies using questionnaires, for example, may be confounded by differences in illness reporting rates, which are likely to vary at different levels of infant morbidity.

The aim of this study was to examine the relation between maternal age and lower respiratory morbidity in a well-controlled study conducted in Tucson, Arizona. The Tucson Children's Respiratory Study was designed as a population-based study to examine the risk factors for lower respiratory illnesses in infants. The study included chronic obstructive pulmonary disease (COPD) and asthma. Over 1,200 infants were born, and accurate records of birth, and accurate records of lower respiratory tract illnesses were kept by the study nurses.

### MATERIALS AND METHODS

Detailed accounts of the methods of enrollment of study subjects, and the prevalence of lower respiratory illnesses during the first year of life, have been published previously (5). Of all mothers who gave birth in Tucson, Arizona, who gave birth during the entire year from October 1984 to October 1985, on days when

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Abbreviations: CI, confidence interval; OR, odds ratio.

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race. The causes for this increased risk for infants of younger mothers have not been elucidated. Some authors stress the possible role of biological factors, especially those affecting fetal development during pregnancy (3), whereas others suggest that mothering skills and child-rearing practices may explain the reported associations (4).

A better understanding of the factors that enhance postneonatal mortality among younger mothers could come from studying the relation between maternal age and postneonatal morbidity. Unfortunately, very few such studies are available. This is probably attributable to the difficulties in performing well-controlled longitudinal studies during infancy. Studies based on maternal questionnaires, for example, may be biased by differences in illness and symptom reporting which are likely to occur among mothers of different levels of education.

The aim of this report is to examine the relation between maternal age and respiratory morbidity during the first year of life in a well-controlled, longitudinal study conducted in Tucson, Arizona. The Tucson Children's Respiratory Study (5, 6) has been designed as a prospective investigation of the risk factors for lower respiratory tract illnesses in infancy and their relation to chronic obstructive airway diseases later in life. Over 1,200 infants were enrolled at birth, and accurate records of lower respiratory tract illnesses occurring during infancy were kept by their pediatricians and study nurses.

#### MATERIALS AND METHODS

Detailed accounts of the study design, methods of enrollment, characteristics of the study subjects, and methods used to ascertain the presence of lower respiratory tract illnesses during infancy have been published previously (5, 6). The study nurses contacted all mothers who used the services of a health maintenance organization in Tucson, Arizona, who gave birth to a healthy baby during the enrollment period (May 1980–October 1984) and who were in the hospital on days when the nurses were available (usu-

ally 6 days a week). Healthy newborns were considered to be those who did not require oxygen for more than 6 hours after birth, had no major congenital anomalies, and had no symptomatic heart disease or severe systemic disease. A total of 1,246 infants (78 percent of those contacted) were enrolled. Since most families have medical insurance available through their employer, the great majority of the population may be considered middle class. Data on maternal age, maternal smoking habits, number of previous births, maternal education, marital status, ethnic origin, and birth weight were obtained at birth.

For this analysis, mothers were divided into five groups according to their age at the time of delivery: less than 21, 21–25, 26–30, 31–35, and more than 35 years. Initially, we intended to classify mothers in similar 5-year intervals, but starting with an age group of less than 20 years, as reported by others (2). However, because our study was based on families who used a health maintenance organization and because very young mothers are less likely to have this type of medical insurance, the number of mothers aged less than 20 was very small. This made results of risk analysis for this maternal age group quite unstable, particularly in stratified analysis. For this reason, children of mothers aged 20 years were added to the youngest maternal age group, and the classification described above was chosen. Results showed the same trends and, when statistically significant, were so with either method.

Mothers were classified as smokers if they reported smoking one or more cigarettes per day. Maternal education was classified as "high" if the woman had completed more than 12 years of formal education and as "low" otherwise. Marital status were classified as "unmarried" if mothers were single, separated, or divorced and as "married" otherwise. Children were classified as "Anglo" if they had at least one white, non-Mexican-American parent and as "Hispanic" if both parents defined themselves as being of Mexican-American origin. The few subjects who belonged to other ethnic groups ( $n = 55$ ) were classified as "other."

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Data on feeding patterns were obtained both prospectively from well baby visits and retrospectively from questionnaires completed by parents. Infants were classified as being breast-fed if they had received mother's milk (regardless of whether other foods were given) for at least 1 month. In addition, information on day care was elicited during the child's second year, and parents were asked if the infant had spent 9 or more hours a week in the company of other children. In the same questionnaire, parents were asked if the infant had had physician-diagnosed eczema during the first year of life.

Total serum immunoglobulin E was measured in cord blood for 1,081 infants (86.8 percent) as described earlier (7).

#### Lower respiratory tract illnesses

Parents were instructed to take their child to their pediatrician if the child developed symptoms of lower respiratory illness (deep or "wet" chest cough, wheezing, hoarseness, stridor, or shortness of breath). To provide this service to its clients, the health maintenance organization charged them only a minimal fee for each visit. At the time of the acute illness, the physicians completed a standardized form on the presence or absence of a number of signs and symptoms. The study nurses, located in the pediatrician's offices, obtained additional historical information: cultures for viruses, mycoplasma, and chlamydia; and blood samples (6). Medical records were checked periodically to ensure that most or all lower respiratory tract illnesses were included. For the purpose of this study, only the first lower respiratory tract illness occurring during the first year of life was considered. Reports by the pediatricians or by parents at the time of the acute illness were used to classify lower respiratory tract illnesses as "wheezing" and "nonwheezing."

Only the 1,022 infants (82.0 percent) who remained under the care of the health maintenance organization pediatricians for the entire first year of life have been included (6). Because selective withdrawal from the study could be a source of bias, all subjects

who stopped using the health maintenance organization pediatricians were excluded, and this included infants who had lower respiratory tract illnesses while still under their care.

#### Data analysis

The associations between maternal age and wheezing and nonwheezing lower respiratory tract illnesses were assessed for all infants at risk bivariate and after controlling for potential confounders. Odds ratios were used instead of ratios between incidences (or "relative risks") to allow for comparisons of results obtained from raw data analyses and those obtained from logistic regressions. Confidence intervals and statistical significance for trends in proportions were calculated by using the methods described by Rothman (8). A categorical logistic model was used to assess the independent effects of maternal age after simultaneously controlling for confounders (8, 9). This technique avoids a priori assumptions about the form of the relation between independent and dependent variables. Relevant independent variables (i.e., maternal age and birth rank) were stratified, and each stratum was then introduced as an independent regression variable. The risk of having lower respiratory tract illnesses in each stratum was compared with that of a predefined reference group, either the lowest or the highest for each variable; this baseline stratum has an odds ratio of unity. To assess linear trends for predictor variables, the logarithms of the odds ratios obtained from the logistic regression were plotted against the different levels of the predictor variable. If the observed data points approached linearity, the weighted least squares regression technique proposed by Rothman (8) was applied, taking the inverse of the variance of the odds ratios as the weight for each data point (stratum). Values used in this regression for each maternal age group were the mean age for that group. Likewise, the mean rank was used for infants born fourth or higher in rank. Because the outcome was a ratio, confidence intervals around the regression line were

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TABLE 1. Comparison of subjects who were followed for the first year of life and those withdrawn from the study, Tucson, Arizona, 1980-1984\*

	Maternal age (years)	Maternal smoking (% ≥1 cigarette/	Marital status (% married)	Day care use (%)	Breast feeding (% breast-fed)	Ethnicity		Maternal education (% <12 years)	Rank (%)			
						Anglo	Hispanic	Other	1	2	3	≥4

TABLE 1. Comparison of subjects who were followed for the first year of life and those withdrawn from the study, Tucson, Arizona, 1980-1984\*

	Maternal age (years)†	Maternal smoking (% ≥ 1 cigarette/day)	Marital status (% married)	Day care use (%)	Breast feeding (% breast-fed)	Ethnicity			Maternal education (% <12 years)	Rank (%)			
						Anglo	Hispanic	Other		1	2	3	≥4
Participants (n = 1,022)	27.6 ± 0.1	17.6	92.7	47.5	83.8	83.9	75.7	69.1	29.8	91.8	94.7	94.7	71.5
Withdrawn (n = 224)	25.7 ± 0.3	18.0	84.7	42.7	80.5	16.1	24.3	30.9	40.9	8.2	5.3	5.3	28.5
p value	<0.0001	0.9	<0.001	0.4	0.5	0.001			0.001				<0.0001

\* Not all values were obtained from the total number of participants or those dropped from the study because of missing data.

† Mean ± standard error.

always calculated using the logarithmic scale (8). Deviation from linearity was assessed by comparing goodness of fit  $\chi^2$  for linear and nonlinear models, as previously described (9, 10). In all logistic analyses, factors that could potentially modify or confound the relation under study were included in the analysis regardless of their statistical significance (8). All *p* values less than 0.05 were considered to be significant.

The study was approved by the Human Subjects Committee of the University of Arizona. Informed consent was obtained from parents at the time of enrollment.

## RESULTS

Comparison of infants who were followed for the first year of life with those withdrawn from the study showed some important differences between these two groups (table 1). Mothers of participants were significantly older and better educated than were mothers of nonparticipants. In addition, Anglo children were significantly more likely to be followed for the entire first year of life than were Hispanic children and those of other ethnic origins. Finally, children with three or more siblings were significantly more likely to be withdrawn from the study than was the rest of the population.

Table 2 shows the relation between maternal age and other possible determinants of lower respiratory tract illnesses in the first year of life. Younger mothers tended to smoke more and to use day care facilities less for their children than did older mothers, although the associations did not reach statistical significance. They were also less likely to be Anglo or married, or to breast-feed than were older mothers. As expected, the proportion of mothers with more than 12 years of education increased significantly with maternal age, as did mean birth weight and rank (see below).

A total of 339 infants (33.2 percent) had lower respiratory tract illnesses during the first year of life. Information on symptoms during a lower respiratory tract illness was available for 285 infants (84.1 percent of all lower respiratory tract illnesses). Wheezing

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TABLE 2. Relation between maternal age and other possible determinants of lower respiratory tract illnesses for 1,022 infants studied in Tucson, Arizona, 1980-1984

Maternal age (years)	Maternal smoking (% $\geq 1$ cigarette/day)	Marital status (% married)	Day care use (%)	Breast feeding (% breast-fed)	Ethnicity			Maternal education (% <12 years)	Birth weight (kg) (mean $\pm$ standard error)
					Anglo	Hispanic	Other		
<21 (n = 54)	24.1	57.4	29.2	75.0	77.8	18.5	3.7	81.5	3.35 $\pm$ 0.06
21-25 (n = 302)	19.6	92.6	48.2	77.9	78.8	16.9	4.3	42.2	3.40 $\pm$ 0.03
26-30 (n = 395)	17.7	95.9	49.5	87.6	84.6	11.9	3.5	22.8	3.52 $\pm$ 0.02
31-35 (n = 227)	13.7	95.5	47.7	87.4	84.6	11.9	3.5	15.9	3.53 $\pm$ 0.03
>35 (n = 44)	15.9	93.0	44.2	81.8	93.2	4.5	2.3	15.9	3.54 $\pm$ 0.07
p value	0.30	<0.0001	0.12	0.003	0.30			<0.0001	0.002

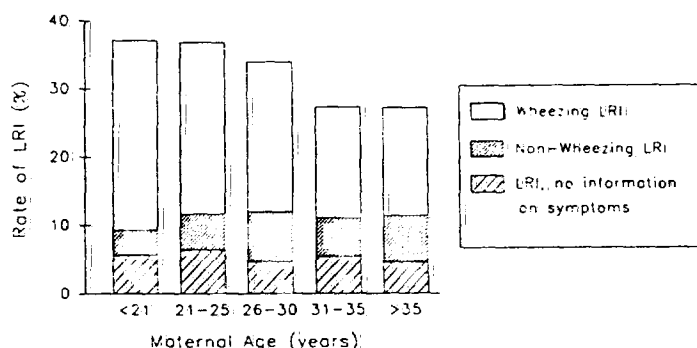


FIGURE 1. Relation between incidence of lower respiratory tract illnesses (LRI) during the first year of life and maternal age in 1,022 infants in Tucson, Arizona, between 1980 and 1984. Numbers of subjects for the five groups were: 54, 302, 395, 227, and 44 for infants of mothers aged less than 21, 21-25, 26-30, 31-35, and greater than 35, respectively.

during a lower respiratory tract illness was ascertained directly by the pediatrician during physical examination in over 90 percent (200 of 222) of cases. For the remaining 22 lower respiratory tract illnesses, wheezing was reported to the pediatricians by parents.

There was a significant, inverse relation between incidence rate of lower respiratory tract illnesses in the first year of life and maternal age (figure 1;  $\chi^2$  for trend = 5.5,  $p$  = 0.02). A more detailed examination of figure 1 reveals that the incidence of non-wheezing lower respiratory tract illnesses was not associated with maternal age: rates for children of mothers aged less than 21, 21-25, 26-30, 31-35, and more than 35 years were 3.7, 5.3, 7.3, 5.7, and 6.8 percent, respectively ( $\chi^2$  for trend = 0.45,  $p$  = 0.5). The association between lower respiratory

tract illnesses and maternal age was mainly due to the significant decrease in incidence rate of wheezing lower respiratory tract illnesses with increasing maternal age. With children of mothers aged more than 35 years as the reference category, the risk of having a wheezing lower respiratory tract illness during the first year of life was 2.0 times higher among infants of mothers aged less than 21 years; 1.8 times higher among infants of mothers aged 21-25; and 1.5 times higher among infants of mothers aged 26-30. The odds ratio for infants of mothers aged 31-35 was only 1.03. A  $\chi^2$  for linear trend was highly significant both when all five strata were included ( $\chi^2$  = 7.6;  $p$  = 0.006) and when maternal age groups 31-35 years and more than 35 years were combined ( $\chi^2$  = 7.7;  $p$  = 0.005). For these rea-

sons, these two groups were included in subsequent analyses.

Trends for the lower respiratory tract illnesses were similar for both sexes, but only for males was there a significant relation with decreasing maternal age. A significant relation was observed for nonwheezing lower respiratory tract illnesses and maternal age (figure 2, not shown).

The incidence rate of lower respiratory tract illnesses was related to birth order (table 4, last column;  $\chi^2$  for trend = 11.2,  $p$  = 0.001). When compared with the risk of having a wheezing lower respiratory tract illness in the first year of life, the risk was 1.2, 1.7, and 1.6 times higher for first-born, second-born, and third-born children, respectively. The risk was also higher for older children in the family, respectively, older than 1 year, 1-2 years, and 2-3 years (Kendall's  $\tau$  for non-

TABLE 3. Incidence of lower respiratory tract illnesses by maternal age

Maternal age (years)	Incidence of LRI (%)
<21	42.0
21-25	40.0
26-30	37.0
>30	30.0

\* LRI, lower respiratory tract illness.  
† Odds ratios were calculated relative to the reference category (maternal age >30 years).

TABLE 4. Rate of wheezing lower respiratory tract illnesses by maternal age

Maternal age (years)	Rate of wheezing LRI (%)
<21	28.0
21-25	25.0
26-30	22.0
>30	15.0
Total	20.0

\* Numbers in parentheses.

sons, these two groups were merged in all subsequent analyses.

Trends for the incidence of wheezing lower respiratory tract illnesses to increase with decreasing maternal age were seen for both sexes, but only reached statistical significance in males (table 3). No significant relation was observed between incidence of nonwheezing lower respiratory tract illnesses and maternal age for either sex (data not shown).

The incidence rate of wheezing lower respiratory tract illnesses was linearly correlated with birth order of the proband (table 4, last column;  $\chi^2$  for trend = 5.8,  $p = 0.016$ ). When compared with firstborn children, the risk of having a wheezing lower respiratory tract illness in the first year of life was 1.2, 1.7, and 1.6 times higher for infants born second, third, or fourth or higher in the family, respectively. However, not surprisingly, older mothers tended to have more children than did younger mothers (Kendall's  $\tau_b$  nonparametric correlation be-

tween birth rank and maternal age = 0.24,  $p < 0.0001$ ). Hence, we reexamined the relation of incidence of wheezing lower respiratory tract illnesses to both maternal age and birth rank after stratification by the other variable (table 4). Incidence of wheezing lower respiratory tract illnesses was associated with maternal age within all four categories of birth rank, and the rank-adjusted  $\chi^2$  for trend was 13.1,  $p = 0.0003$ , and thus was stronger than that obtained using the raw data. Incidence of wheezing lower respiratory tract illnesses was associated with rank within all categories of maternal age, except among children of mothers aged greater than 30 years. After adjustment for maternal age, trend  $\chi^2$  was 11.5 ( $p = 0.0007$ ), which was also stronger than that obtained from the raw data.

Nonwheezing lower respiratory tract illnesses were unrelated to maternal age after maternal education and birth rank were controlled for.

A categorical logistic analysis (see Mate-

TABLE 3. Incidence (%) of wheezing lower respiratory tract illnesses during the first year of life for 1,022 infants by maternal age and sex, Tucson, Arizona, 1980-1984\*

Maternal age (years)	Males				Females			
	No.	Wheezing LRIs†		Odds ratio†	No.	Wheezing LRIs		Odds ratio
		%	p value			%	p value	
<21	27	29.6		2.5	27	25.9		1.6
21-25	138	29.0		2.4	164	22.0		1.3
26-30	205	22.0		1.6	190	22.1		1.3
>30	130	14.6		1.0	141	17.7		1.0
			0.004				0.29	

\* LRI, lower respiratory tract illnesses.

† Odds ratios were calculated using infants whose mothers were >30 years old as reference.

TABLE 4. Rate of wheezing lower respiratory tract illnesses (in %) during the first year of life for 1,022 infants by maternal age and by birth rank, Tucson, Arizona, 1980-1984

Maternal age (years)	Rank				
	1	2	3	≥4	Total
<21	25.0 (48)*	50.0 (4)	50.0 (2)	0.0 (0)	27.8 (54)
21-25	20.7 (164)	28.7 (101)	33.3 (30)	42.9 (7)	25.2 (302)
26-30	16.0 (189)	24.1 (133)	28.3 (53)	40.0 (20)	22.0 (395)
>30	16.0 (81)	12.7 (102)	23.7 (59)	13.8 (29)	16.2 (271)
Total	18.9 (482)	22.4 (340)	27.8 (144)	26.8 (56)	21.7 (1,022)

\* Numbers in parentheses, number of subjects.

rials and Methods) was performed to assess whether other possible confounders could explain the relation between maternal age and risk of having lower respiratory tract illnesses. The following predictor variables were thus added to the model together with maternal age and birth rank: maternal education (12 years or less or more than 12 years); feeding practices (bottle-fed or breast-fed); birth weight; day care (less than 9 hours per week or more than 9 hours per week in the company of other children); marital status (married or unmarried); ethnicity (Hispanic, Anglo, or other); sex; and maternal smoking (nonsmoker or more than one cigarette per day).

Figure 2 shows the odds ratios of having a wheezing lower respiratory tract illness for different maternal ages and the weighted, least squares linear regression fitted to the odds ratios. When compared with infants of mothers aged more than 30 years, adjusted odds ratios were 2.4 (95 percent confidence interval (CI) 1.8–3.1) for infants whose mothers were less than age 21 years ( $p < 0.0001$ ); 1.8 (95 percent CI 1.4–2.3) for infants whose mothers were age 21–25 ( $p < 0.0001$ ); and 1.4 (95 percent CI 1.1–1.6) for infants whose mothers were age 26–30 ( $p <$

0.001). The same type of analysis was performed by using odds ratios for birth rank obtained from the categorical logistic regression. When compared with those for first-born children, odds ratios were 1.4 (95 percent CI 1.1–1.7) for infants born second ( $p = 0.002$ ); 1.8 (95 percent CI 1.3–2.4) for those born third ( $p < 0.001$ ); and 2.2 (95 percent CI 1.5–3.3) for infants born fourth or higher in rank ( $p < 0.001$ ). In addition to maternal age and birth rank, the following variables were independent risk factors for wheezing lower respiratory tract illnesses: maternal smoking (odds ratio (OR) = 1.7, 95 percent CI 1.1–2.5,  $p = 0.01$ ); use of day care facilities (OR = 1.4, 95 percent CI 1.0–2.0,  $p = 0.02$ ); being Hispanic (OR = 1.6, 95 percent CI 1.0–2.6,  $p = 0.04$ ); and being an unmarried mother (OR = 1.8, 95 percent CI 1.0–3.2,  $p = 0.06$ ).

There was still no significant relation between maternal age and risk of having non-wheezing lower respiratory tract illnesses after addition of the above mentioned variables to a logistic model.

There was no significant relation between cord serum immunoglobulin E levels and either maternal age or birth rank. Likewise, the development of eczema during the first

year of life was not associated with birth rank and occurred in infants of

## DISCUSSION

In previous reports, we have shown that factors such as feeding habits (11), room sharing (12), cord blood IgE levels (13), and lung structure (14) are associated with lower respiratory tract illnesses in those associated with the first year of life. In this study, we have added to the above list a new factor, maternal age, which is linearly associated with the risk of lower respiratory tract illnesses. The relation between maternal age and wheezing lower respiratory tract illnesses was also stronger than that between maternal age and non-wheezing lower respiratory tract illnesses.

Our results suggest that lower respiratory tract illnesses are indirectly related to the susceptibility to infection, not to non-wheezing lower respiratory tract illnesses. Because a viral etiology is the cause of the vast majority of lower respiratory tract illnesses (6), we hypothesize that the susceptibility to lower respiratory tract illnesses is not to be related to the susceptibility to infection in the first year of life. We would expect the lower respiratory tract illnesses to be inversely related to the risk of infection. This finding that factors such as room sharing, increased incidence of wheezing lower respiratory tract illnesses in the first year of life, and the reported that infants in the room with other children are at a higher risk of developing lower respiratory tract illnesses during the first year of life (12). Room sharing is a risk factor for viral respiratory infections independent of the risk of infection associated with it.

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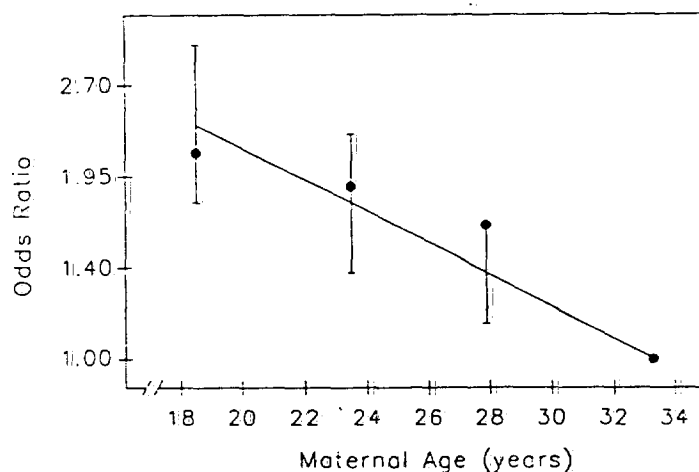


FIGURE 2. Odds ratio of having wheezing lower respiratory illnesses by maternal age after correction for other risk factors. A total of 1,022 infants were studied between 1980 and 1984 in Tucson, Arizona. The solid line is a weighted, least squares linear regression model fitted to the logarithm of the odds ratios for each maternal age group (less than 21, 21–25, 26–30, and greater than 30 years, respectively). Points, mean maternal age for each group; bars, 95% confidence interval around the regression for each odds ratio.



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## DISCUSSION

In previous reports based on this population, we have shown that maternal smoking habits (11), room sharing and feeding practices (12), cord blood immunoglobulin E (13), and lung structure and function (14) are associated with the risk of developing lower respiratory tract illnesses (especially those associated with wheeze) during the first year of life. In this study, we add to the above list a new, important risk factor: younger maternal age. The risk increased linearly with decreasing maternal age, but the association was limited to wheezing lower respiratory tract illnesses; there was no relation between maternal age and non-wheezing lower respiratory tract illnesses. It was also stronger for males than for females.

Our results suggest that factors directly or indirectly related to maternal age increase the susceptibility of infants to wheezing, but not to nonwheezing respiratory illnesses. Because a viral etiology was ascertained for the vast majority of these two types of illnesses (6), we hypothesize that such factors ought not to be related to an increased general susceptibility to viral infection during the first year of life. If this were the case, we would expect the incidence of both types of lower respiratory tract illnesses to be inversely related to maternal age. This hypothesis is further supported by our previous finding that factors known to increase the risk for infection are associated with an increased incidence of both wheezing and non-wheezing lower respiratory tract illnesses in the first year of life (12). Specifically, we reported that infants who slept in the same room with other people were at increased risk of developing lower respiratory tract illnesses during the first 4 months of life (12). Room sharing is likely to increase the risk of viral respiratory infection in general, independent of the specific symptoms associated with it.

Very few studies have addressed the rela-

tion between maternal age and infant morbidity. Most studies have focused on infants of adolescent mothers, the prevalent idea being that these infants have more health problems than do infants born to older mothers (15). Outcome variables for most of these retrospective studies have been general indices of disease frequency such as number of hospitalizations in the first 3 (16) or 5 years of life (17). This detracts from the possibility of comparing their results with those reported herein. A report by Ogston et al. (18) is the only longitudinal study of which we are aware that is comparable with ours. These authors obtained retrospective information from parents about "respiratory illnesses" (without distinguishing between upper and lower respiratory illnesses) during the first year of life in over 1,500 infants born to primigravidas in Dundee, Scotland. They found a significant inverse relation between maternal age and incidence of respiratory illnesses during the first year of life, but the statistical significance disappeared after controlling for maternal smoking and other confounding factors. More recently, Schwartz et al. (19) studied a large sample (over 4,500 subjects) of the US population between the ages of 6 months and 11 years. They found a significant inverse relation between maternal age and prevalence of physician-diagnosed asthma, as reported by parents. This relation was still significant after controlling for age, sex, race, and birth weight. Prevalence of wheezing was also inversely related (albeit not significantly) to maternal age (19). The authors also found that maternal age appeared to be a stronger predictor of asthma for boys than for girls (19), much as we found that maternal age was a better predictor of wheezing lower respiratory tract illnesses in boys than in girls. The relation between lower respiratory tract illnesses and the development of asthma is very complex, but our results and those of Schwartz et al. (19) would indicate that young motherhood may be a common predisposing factor for both of these illnesses.

This predisposition does not seem to be mediated by an increased risk for developing

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allergies early in life in children of younger mothers. We found no association between maternal age and either cord serum immunoglobulin E levels or the risk of having eczema during the first year of life. Likewise, we were unable to confirm the finding by Strachan (20) that atopy (as assessed by cord serum immunoglobulin E levels or incidence of eczema in the first year of life) is more common in firstborn children. The different ages at which the subjects were studied and the different indices of atopy used in both studies may explain these discrepancies.

It is reasonable to argue that maternal age may be a proxy for some unknown social factor that we may have failed to consider in our analyses. We did not adjust our results directly for an index of social class derived from paternal or maternal occupation because it has been previously shown (21) that most of the variability in prevalence of respiratory diseases related to social factors is explained by level of education. More complex parameters of social level are highly correlated with the level of education and add little in statistical power to the analyses. The underrepresentation in our sample of infants from poorer backgrounds also argues against socioeconomic factors as an explanation for our findings. In addition, our results were independent of ethnicity, marital status, feeding practices, and maternal smoking habits, all of which are known to be related to or to be determinants of socioeconomic status. However, we cannot exclude the possibility that other social or environmental conditions (such as nutrition, quality of the house, and health status of the mother, among others) may have confounded the associations reported herein.

Perhaps more subtle aspects of the maternal-infant relationship are influenced by maternal age and may explain our findings. It has been suggested that younger mothers may provide a lower quality of care for their children during early infancy than older mothers (1). Jones et al. (22) found that younger mothers were less responsive than older mothers to their newborn infant's needs during the neonatal period.

McAnarney et al. (23) were unable to confirm these findings, but, in a subsequent report, this group of researchers found that younger maternal age was associated with less favorable mothering behaviors when the infant was 9–12 months old (24). Interestingly, experimental studies have shown that mild stressful stimuli (such as subcutaneous injections of saline to suckling rats) may elicit long-term alterations in the mechanical characteristics of the lung (25). Younger mothers may also take less care of themselves during pregnancy and may thus increase the level of stress of the fetus. Naeye (3) suggested that the growth needs of young mothers may compete with the growth needs of their fetuses for available nutrients, and this may be a source of additional fetal stress. Fetal stress that persists for prolonged periods of time is known to be associated with increased endogenous cortisol secretion (26), and prenatal administration of corticosteroids has been shown to depress lung growth (27). These hypothetical pathogenetic mechanisms relating maternal age to fetal and infant stress and to lung development are relevant because we have shown previously that infants who subsequently had wheezing lower respiratory tract illnesses (but not those who only had nonwheezing lower respiratory tract illnesses) had diminished lung function long before any lower respiratory tract illness developed (14). We suggested that smaller lungs and/or smaller airways could predispose to wheezing during respiratory tract infections. On reanalyzing those results, we found that size-adjusted maximal expiratory flows at functional residual capacity were significantly correlated with maternal age in male (partial  $r = 0.28$ ;  $p < 0.05$ ) but not in female infants. There was no relation between functional residual capacity and maternal age (Fernando D. Martinez, University of Arizona, unpublished manuscript). This finding is compatible with the stronger relation we found between maternal age and incidence of wheezing lower respiratory tract illnesses in males (table 3). It is thus possible that factors associated with younger maternal age may affect lung development in the children of younger moth-

ers and predispose to obstructive illness.

It is important that we acknowledge that there may have been several sources of bias in our study. First, the respiratory tract illness period that required hospitalization for administration of antibiotics was not enrolled in the study. Second, the low-birth-weight infants with a major neonatal complication were not enrolled. Third, younger mothers may have respiratory tract illnesses more often (28), exclusion of these mothers might perhaps decrease the strength of the reported findings. Fourth, the study included only a single birth cohort, which limited our population to those born in a health care facility. Fifth, the study included only households of low socioeconomic status, which are probably underrepresented in the general population. If anything, this may have biased the socioeconomic findings of this study. Finally, it is possible that this was a significant source of bias. It was a significant finding that the incidence of wheezing lower respiratory tract illnesses was often higher in older mothers than in younger mothers. To explain our results, we suggested a relation between maternal age and lower respiratory tract illnesses, strong enough to reverse the association when present among the children of older mothers.

Finally, we need to acknowledge that older mothers may have children that are less likely to be frightened by the pediatrician for a number of reasons. If this were the case, we would expect the incidence of wheezing lower respiratory tract illnesses to be inversely associated with maternal age, and this was not the case. In addition, the known relation between maternal age and the incidence of wheezing lower respiratory tract illnesses among young children is not likely to be characterized by a linear relationship. The findings of this study suggest that the incidence of wheezing lower respiratory tract illnesses is less among the children of older mothers and less among the children of younger mothers.

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It is important to note that our results may have been influenced by potential sources of bias in our data. Infants who had respiratory troubles during the neonatal period that required supplemental oxygen administration for more than 6 hours were not enrolled in the study (5). However, since low-birth-weight infants and those with neonatal complications are more often born to younger mothers (2) and are more apt to have respiratory infections during infancy (28), exclusion of these infants could perhaps decrease the significance of the reported findings. Likewise, because we limited our population sample to newborns enrolled in a health maintenance organization, households of lower socioeconomic status are probably underrepresented in our study; if anything, this makes it less likely that other socioeconomic factors, uncontrolled for in this study, may explain our results. There was a significant trend for younger mothers to stop using the study pediatricians more often than older mothers. For this tendency to explain our results, however, a direct relation between maternal age and wheezing lower respiratory tract illnesses, strong enough to reverse our findings, should be present among the minority of cases excluded from the analysis.

Finally, we need to consider the possibility that older mothers may be more experienced and thus less troubled by symptoms that may frighten younger mothers and may induce the latter to take their children to the pediatrician for less important illnesses. If this were the case, however, one would expect the incidence of both wheezing and nonwheezing lower respiratory tract illnesses to be inversely associated with maternal age, and this was not apparent in our data. In addition, the known inverse relation between maternal age and postneonatal mortality (2) would argue against overzealousness among younger mothers. In fact, some authors believe that young motherhood may be characterized by precisely opposite shortcomings, i.e., less ability to recognize serious illness and less access to medical care (1).

Clearly, this issue requires further elucidation. However, it is safe to conclude from our data that infants of younger mothers may be at increased risk of having acute obstructive respiratory illnesses and that this may explain, at least in part, their higher postneonatal mortality rates.

In summary, infants born to younger mothers were reported by their pediatricians to develop clinically important signs of bronchial obstruction during viral infections more often than did those of older mothers. This was in part due to the significant association between lower maternal age and prevalence of known risk factors for wheezing lower respiratory tract illnesses. However, the association between maternal age and wheezing lower respiratory tract illnesses persisted after controlling for many of these known risk factors. A better understanding of the factors related to maternal age that predispose infants to develop wheezing lower respiratory tract illnesses may help in the prevention of this important cause of morbidity during the first year of life.

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## Five Cross-sections

Moira Chan-Yeung

Five cross-sections of workers with asthma. The first two questionnaires measured the prevalence of asthma in each of the five cross-sections. The third questionnaire measured the prevalence of asthma in each of the five cross-sections. The fourth questionnaire measured the prevalence of asthma in each of the five cross-sections. The fifth questionnaire measured the prevalence of asthma in each of the five cross-sections.

cross-sections

There have been many studies showing the prevalence of respiratory symptoms in grain workers. The first two studies were cross-sections in all of the ten grain workers in Columbia. Canada. The third study was part of a surveillance study. The fourth study was a cross-section. The fifth study was a cross-section.

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Abbreviations: FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow rate.

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Baghurst, P.A., Tong, S.L., McMichael, A.J., Robertson, E.F., Wigg, N.R., and Vimpani, G.V., "Determinants of Blood Lead Concentrations to Age 5 Years in a Birth Cohort Study of Children Living in the Lead Smelting City of Port Pirie and Surrounding Areas," Arch Environ Health 47(3): 203-210, 1992.

The authors performed an investigation of the determinants of blood lead concentrations (PbB) among 646 Australian children born near a lead smelter. The results of a multiple regression analysis suggested that the associations between PbBs and topsoil lead levels, employment of father at the smelter, parental smoking, behaviors likely to cause ingestion of dirt, and season remained statistically significant.

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## Determinants of Blood Lead Concentrations to Age 5 Years in a Birth Cohort Study of Children Living in the Lead Smelting City of Port Pirie and Surrounding Areas

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**ABSTRACT.** Sources of variation and some principal determinants of blood lead concentration (PbB) were investigated in a cohort of children, followed to age 5 y, who were born near a lead smelter in Port Pirie, South Australia. The child's age and place of residence were the two variables most strongly predictive of PbB. A sharp increase in PbB occurred between 6 and 15 mo of age and was followed by a peak concentration that occurred at approximately 2 y of age, after which PbB steadily and consistently declined. Irrespective of age, the PbBs in children who lived in Port Pirie were significantly higher than levels identified in children who resided outside the city. There was no significant difference in PbB between boys and girls. Elevated PbB at each specific age was associated mainly with increased lead concentrations in the topsoil of the local residential area, employment of the father in the lead industry, parental smoking, and behaviors likely to cause ingestion of dirt. Blood samples taken from children at certain ages and during the warmer months contained more lead than samples obtained during the cooler months. The effects of these determinants on PbB during early childhood were basically consistent in both single and multivariable analyses.

THE ADVERSE EFFECTS of excessive lead exposure on the intellectual, cognitive, and behavioral development of young children have received increased atten-

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tion during the past decade.<sup>1,3</sup> Definitive evidence of neuropsychological effects that result from exposure to low levels of lead continues to be sought in prospective studies of child development. Some epidemiological studies have shown an inverse relationship between blood lead concentrations (PbBs) and early cognitive function,<sup>4,7</sup> and, therefore, the question of how exposure to environmental lead can be reduced in children has become a major public health concern.

Many researchers have described the relationship between PbBs and associated determinants.<sup>8-10</sup> Very limited longitudinal data on the variations and determinants of PbB during early childhood are available. Most data available have been derived from cross-sectional surveys of school-age children and adults or from clinically based groups of young children.

In 1979, the recruiting of pregnant women for a prospective study of lead exposure and its relationship to pregnancy outcome and early childhood growth and development was initiated in the South Australia town of Port Pirie (population 16 000), which is 200 km north-west of Adelaide. The town is located immediately downwind from a large and longstanding lead-smelting facility. Although emissions are now controlled tightly, past activities of the smelter, the use of lead-bearing waste as landfill, and unloading activities at the railhead have left the city with a legacy of extensive environmental contamination with lead, much of it finely particulate and sufficiently mobile to be a problem in dust and topsoil.

The Port Pirie Cohort study is concerned primarily with early childhood physical and neurobehavioral development and the relationship of cumulative lead exposure with each. The study, however, has highlighted the relationship between PbB and socioeconomic status, behavioral factors, and environmental circumstances. Determinants of PbBs in the same cohort have already been described for children who are 2 y of age or younger<sup>11</sup>; this paper, therefore, extends the findings to age 5 y, i.e., just prior to attending school.

## Materials and methods

**Study population.** The children in the cohort were born in the town of Port Pirie or in the surrounding rural area within a radius of approximately 30 km; the rural area included the townships of Laura, Crystal Brook, Port Broughton, and Gladstone. A total of 831 pregnant women were enrolled in the study from May 1979 to May 1981. This number accounted for an estimated 90% of all new pregnancies during this period. Seven hundred twenty-three of the 831 pregnancies were followed to single live births. The numbers of children who remained in the cohort were 646, 607, 585, 556, 530, and 513, and their ages were 6, 15, 24, 36, 48, and 60 mo, respectively. The majority (i.e., approximately 80%) of the children lost to follow up during the 5 y of postnatal study were in families that left the Port Pirie district; a few families discontinued participation. Additional information about the socio-demographic characteristics of the children who remained in the cohort and about those lost to follow up is available elsewhere.<sup>12</sup>

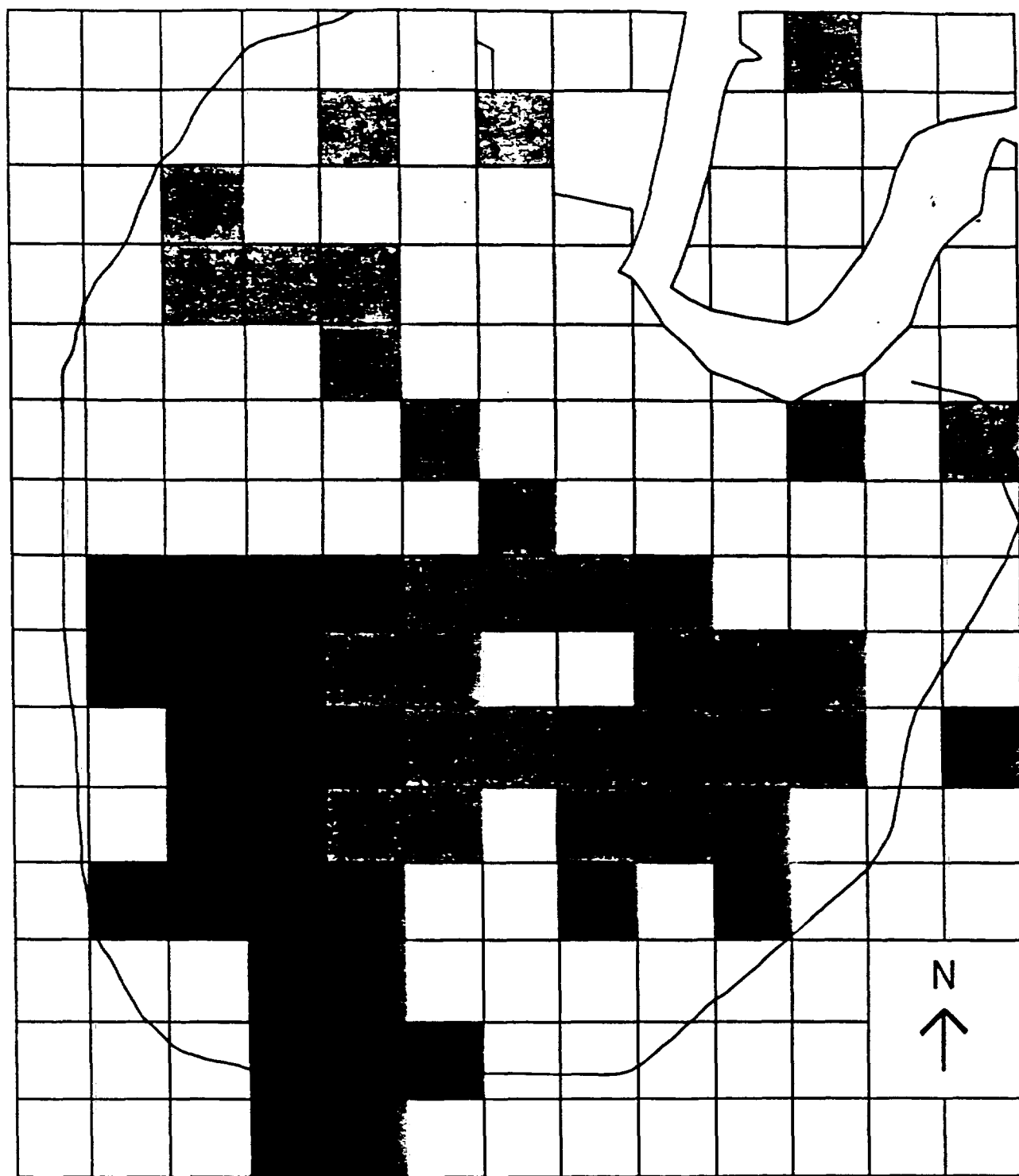
**Data collection.** Capillary blood samples for measurement of PbBs were obtained under standardized conditions and rigorous procedures.<sup>13</sup> Samples were collected from each child at 6, 15, 24, 36, 48, and 60 mo of age. In a separate validation study conducted in a group of 47 Adelaide metropolitan children aged 2-4 y, a close correlation ( $r = .97$ ) was observed between lead concentrations obtained with capillary sampling and with simultaneous venous sampling.<sup>14</sup> At the same time blood samples were collected, the nurse-interviewer also conducted a structured interview and obtained information on a range of demographic, behavioral, and environmental factors.

**Laboratory analysis.** Measurements of PbBs were performed in the Department of Chemical Pathology at the Adelaide Centre for Women's and Children's Health (formerly the Adelaide Children's Hospital). Blood lead concentrations were measured by electrothermal atomization atomic absorption spectrometry.<sup>15</sup> The blood lead assay performed in this cohort study was described previously and was subject to internal and external quality control procedures, and satisfactory results were obtained consistently. A certified commercially prepared product was used to monitor intra-batch accuracy and to ensure uniformity between batches. External quality control, which entailed assay of regularly supplied samples, was maintained by the Standards Association of Australia and the international programs operated by the Health Department of Pennsylvania (USA) and the Wolfson Research Laboratories (Birmingham, UK). Individual PbBs were adjusted to a packed cell volume of 35%.

**Soil and dust lead.** Because the dust-hand-mouth route may be a predominant form of lead exposure during early childhood, the relationship between PbB and three local measures of dust in soil was examined. (1) A survey of lead in topsoil was conducted by the South Australian Health Commission;<sup>16</sup> (2) lead in ceiling dust was surveyed by the Department of Environment and Planning<sup>17</sup> (ceiling dust was chosen because many houses are designed with an airflow through the roof space, and dusts collected between the ceiling rafters are generally representative of dusts deposited during the life of each house); and (3) lead in dust on window-sills<sup>17</sup> was surveyed by the Department of Environment and Planning.

In each survey, soil- or dust-lead values were averaged for 200-m<sup>2</sup>, an area that was defined by a rectangular grid drawn across the residential area of Port Pirie. The average for the appropriate area was then used as a covariate for all children who resided in that area. All three measures were strongly predictive of a child's PbB, but the Health Commission data were more extensive than the others and were, therefore, chosen for all subsequent analyses (Fig. 1). It should be noted that sites sampled by the Health Commission were not random, but focused on homes of children who had unacceptably high PbBs. Thus, the reported concentrations may be overestimates of the general situation within Port Pirie, but the volume of data collected in this manner would have insured that the final summary data closely approximated the true situation, and Figure 1 is





>1000 ppm  
 500-1000 ppm  
 < 500 ppm  
 no data

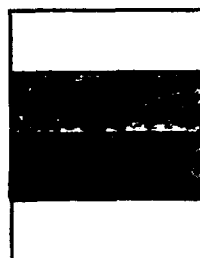


Fig. 1. Distribution of lead in the topsoils of Port Pirie. The grid lines are 400 m apart, and the outer limits of dense housing are indicated by the continuous line.

remarkably similar to the maps published by the Department of Environmental Planning.<sup>17</sup> Nevertheless, it was prudent to use the soil data in a categorized form, which avoided assumptions of curvilinearity and allowed inclusion of the children who lived outside Port Pirie and for whom there were no soil lead data.

Analysis of lead concentrations in the samples collected by the Health Commission was conducted by flame atomic absorption spectrometry, for which the ethylenediamine tetraacetic acid (EDTA) extraction method was used.<sup>18</sup>

**Other variables.** Social status was quantified by a scale proposed by Daniel<sup>19</sup> and was based on the perceived prestige of the father's occupation. Paternal employment at the smelter was used as a separate variable. Parental smoking was defined as the number of parents who smoked (i.e., 0, 1, or 2). Behaviors likely to lead to ingestion of dirt included mouthing activity, eating dirt, and/or sucking fingers. Each behavior was categorized by reported frequency, i.e., often, a little, or never. Education was estimated as the number of years the child's father/mother had attended secondary school.

In the town of Port Pirie and its surrounding rural area, some families collect rainwater runoff from rooftops and store it in tanks for drinking, cooking, or other domestic uses. This supply can be contaminated by lead-containing dust; therefore, use of rainwater was employed as one of the variables that might influence a child's lead burden.

Because exposure to environmental lead may vary during the seasons, a simple variable to indicate whether each child's birthday occurred in the warmer or cooler months of the year was also included. April–October were considered cooler months, and November–March were the warmer months.

**Statistical analysis.** Because blood lead concentrations are typically skewed, analysis was performed on the natural logarithm of PbB, and all means reported are geometric and not arithmetic. Multiple regression analyses were conducted in an attempt to construct an appropriate model to explain the variation in PbBs. Residual analysis supported the regression model assumptions of normality.

The final results of the multiple regression analysis were reported as percentage differences. For example, if the estimate of the regression coefficient (of log PbB) for girls was  $-.057$  relative to a value of 0 for boys, this would be equivalent to concluding that girls have a PbB that is  $100[\exp(-.057) - 1] = -5.6\%$  "above" (i.e., 5.6% below) that of their male counterparts, assuming values for all other independent variables remain the same.

## Results

Variations in geometric mean PbB with respect to age, gender, and location of residence are indicated in Figure 2. There was a considerable increase in PbB between the ages of 6 and 15 mo, and the peak concentration observed (Port Pirie, 25.1  $\mu\text{g/dl}$ ; non-Port Pirie, 17.4  $\mu\text{g/dl}$  [conversion factor for SI units: 1.0  $\mu\text{mol/l} =$

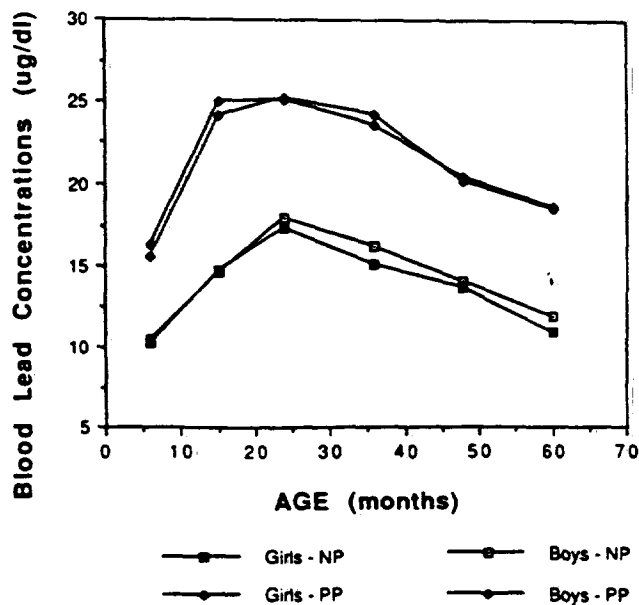


Fig. 2. Geometric mean blood lead concentration, by age, sex, and location of residence. (PP = Port Pirie; NP = outside Port Pirie).

20.7  $\mu\text{g/dl}$ ) occurred at 2 y of age and was followed by a subsequent slow and steady decline at later ages. However, the mean PbB in children aged 5 y (Port Pirie, 18.6  $\mu\text{g/dl}$ ; non-Port Pirie, 11.5  $\mu\text{g/dl}$ ) remained significantly higher than the levels recorded at birth (Port Pirie, 9.4  $\mu\text{g/dl}$ ; non-Port Pirie, 5.7  $\mu\text{g/dl}$ ).

The PbBs in children who lived in Port Pirie were considered higher (53.8%–68.5%) at all ages than in children who resided outside the city; the maximum difference occurred at 15 mo of age. At no age was there a statistically significant difference between boys and girls.

There was an inverse gradient in geometric mean PbB (Table 1) as social status increased in each age group ( $p < .01$ ). The PbBs in children whose parent(s) smoked tended to be 1.7–3.0  $\mu\text{g/dl}$  (10%–19%) higher than in children whose parents did not smoke. Mouthing activities, eating dirt, and sucking fingers were associated with elevated PbBs.

There was a strong relationship between a child's PbB and the father's employer. The PbBs of children whose fathers were employed in the smelter (17.2–25.4  $\mu\text{g/dl}$ ) were significantly higher than those of children whose fathers were employed elsewhere (10.6–20.9  $\mu\text{g/dl}$ ). At each age there was a clear, positive gradient in mean PbB (11.1–28.3  $\mu\text{g/dl}$ ), relative to local soil lead concentrations. The gradients were stronger at age 6–15 mo than at all subsequent ages. Each age-specific gradient in mean PbB "relative to," including lead-exposure employment of parent and topsoil lead levels, was highly statistically significant ( $p < .01$ ). At each age the mean PbB was higher during the warmer months and lower in cooler months; this difference was statistically significant at ages 6 mo ( $p = .057$ ), 15 mo ( $p = .001$ ), 36 mo ( $p = .005$ ), and 48 mo ( $p = .036$ ).

The results of multiple regression analysis (Table 2) showed that the associations between PbBs and topsoil lead levels, employment at the smelter, parental smoking, behaviors likely to cause ingestion of dirt, and season remained statistically significant. Nevertheless, apparent effects of gender, work duration of mother, parental secondary education and occupation, and rain-water use on mean PbB were not found in this multiple regression model.

### Discussion

The results indicated that there was a significant increase in either exposure to, or uptake of environmental lead in infancy. The peak mean PbB appeared to occur at age 2 y, and there was a subsequent slight but

steady decline thereafter. These findings corroborate the reports from several other community-based studies conducted in the United States and Europe, each of which showed a peak in mean PbB at 2-3 y of age.<sup>20,21</sup> Although the Second National Health and Nutrition Examination Survey in the United States<sup>22</sup> and a few other studies<sup>23,24</sup> did not report a peak in mean PbB at this age exactly, it is apparent that the reported values in infancy were considerably higher than those recorded by their maternal age group and that a rise in PbB must have occurred soon after birth, when cord blood lead is quantitatively similar to maternal PbB. A definitive explanation for this phenomenon remains elusive, but it is likely to involve an enhanced ability to absorb lead and/or an increased ingestion of lead that

Table 1.—Variations in Blood Lead Concentrations, by Gender, Season, Socioeconomic Status, Parental Smoking, Behaviors, Workplace of Father, and Topsoil Lead Levels

Factors	Age (mo)					
	6 (n = 646)	15 (n = 607)	24 (n = 585)	36 (n = 556)	48 (n = 530)	60 (n = 513)
Gender						
Male	14.0 (1.02)	20.4 (1.02)	21.4 (1.02)	19.6 (1.02)	16.4 (1.02)	14.6 (1.02)
Female	14.5 (1.02)	21.1 (1.02)	20.8 (1.02)	19.1 (1.02)	16.4 (1.02)	14.3 (1.03)
Season						
Warmer	14.8 (1.02)	22.1 (1.02)	21.3 (1.02)	20.2 (1.02)	17.0 (1.03)	14.7 (1.03)
Cooler	13.9 (1.02)	19.9 (1.02)	21.0 (1.02)	18.7 (1.02)	16.0 (1.02)	14.2 (1.02)
Socioeconomic status						
Lowest	17.2 (1.07)	24.0 (1.08)	24.7 (1.08)	21.9 (1.08)	19.5 (1.07)	18.1 (1.07)
Low	16.6 (1.03)	25.2 (1.03)	25.5 (1.03)	23.0 (1.03)	19.6 (1.03)	17.6 (1.03)
Middle	14.2 (1.04)	19.8 (1.04)	19.8 (1.03)	19.1 (1.03)	16.2 (1.03)	14.0 (1.03)
High	13.2 (1.03)	19.3 (1.03)	19.8 (1.03)	17.9 (1.03)	15.2 (1.03)	13.2 (1.04)
Highest	12.3 (1.04)	18.2 (1.04)	18.7 (1.04)	16.2 (1.04)	13.7 (1.04)	12.0 (1.04)
Parental smoking						
None	13.5 (1.03)	19.0 (1.03)	19.4 (1.02)	17.8 (1.02)	15.1 (1.03)	13.4 (1.03)
One	14.3 (1.03)	21.1 (1.03)	21.5 (1.02)	19.9 (1.03)	16.8 (1.03)	14.8 (1.03)
Both	15.0 (1.03)	22.5 (1.03)	23.1 (1.03)	21.1 (1.03)	18.4 (1.03)	16.4 (1.04)
Mouthing activity						
No	-	20.5 (1.06)	19.9 (1.02)	18.6 (1.02)	16.0 (1.02)	14.2 (1.02)
Yes	-	20.8 (1.02)	22.0 (1.02)	21.0 (1.03)	18.2 (1.04)	15.8 (1.06)
Dirt eating						
No	-	20.2 (1.04)	20.6 (1.02)	18.8 (1.02)	16.3 (1.02)	14.4 (1.02)
Yes	-	20.9 (1.02)	21.9 (1.02)	22.4 (1.04)	18.6 (1.06)	14.9 (1.08)
Finger sucking						
Never	-	20.8 (1.02)	20.6 (1.02)	18.8 (1.02)	16.1 (1.02)	14.0 (1.02)
Occasionally	-	21.2 (1.03)	22.1 (1.03)	20.6 (1.03)	16.8 (1.03)	15.3 (1.03)
Often	-	19.3 (1.06)	22.2 (1.08)	19.3 (1.05)	17.6 (1.07)	15.5 (1.10)
Father's job						
Non-Port Pirie	10.6 (1.03)	15.4 (1.03)	16.4 (1.03)	15.3 (1.02)	12.9 (1.03)	11.1 (1.03)
Nonsmelter	14.5 (1.02)	20.9 (1.03)	20.8 (1.03)	19.4 (1.03)	17.2 (1.03)	14.8 (1.03)
Smelter	17.2 (1.02)	25.3 (1.02)	25.4 (1.02)	23.2 (1.02)	19.3 (1.02)	17.7 (1.02)
Soil lead (ppm)						
Non-Port Pirie	11.1 (1.03)	15.5 (1.03)	16.9 (1.03)	15.1 (1.02)	13.0 (1.03)	11.1 (1.03)
< 500	14.7 (1.03)	22.0 (1.03)	22.2 (1.03)	21.2 (1.03)	17.7 (1.03)	16.5 (1.03)
< 1 000	15.8 (1.03)	23.5 (1.03)	23.3 (1.03)	21.7 (1.03)	18.4 (1.03)	16.5 (1.03)
> 1 000	18.7 (1.03)	28.3 (1.03)	26.7 (1.03)	25.1 (1.03)	22.0 (1.03)	18.8 (1.04)
No data†	13.3 (1.10)	20.8 (1.11)	19.9 (1.08)	19.8 (1.09)	15.4 (1.13)	13.0 (1.17)

Note: Geometric standard errors appear within parentheses.

\* $p < .01$ .

† $p < .05$ .

‡Number of children for whom lead data were unavailable are 17, 20, 20, 16, 13, and 10 at the ages of 6, 15, 24, 36, 48, and 60 mo, respectively.

Table 2.—Relative Shifts (%) of Blood Lead Concentrations, Estimated by Multiple Regression Analyses

Factors (reference categories)	Categories	Age (mo)					
		6	15	24	36	48	60
Demography							
Gender (males)	Females	-2.6	1.9	-4.3	-4.8	1.4	-5.6
Secondary education (y)							
Father ( $\leq 3$ )	> 3	7.3	-4.6	-5.8	-4.7	-5.2	-6.2
Mother ( $\leq 3$ )	> 3	3.7	-1.1	0.2	-2.0	-1.9	4.1
Socioeconomic status (Lowest)							
	Lower	-0.3	2.1	-7.5	-11.2	-10.3	2.0
	Middle	-0.3	-4.4	-21.3*	-16.3	-11.3	-8.6
	Higher	-8.7	-1.0	-17.0	-16.0	-13.6	-8.2
	Highest	-13.5	-6.6	-20.3*	-22.7*	-19.6	-13.4
Occupation							
Mother (lower)	Middle	-10.8	1.5	3.7	-6.7	5.4	-1.1
	Higher	-0.4	0.8	-2.0	-7.9	-3.1	-10.2
Father (lower)	Middle	1.1	-6.2	1.3	0.4	-2.2	1.9
	Higher	-3.4	-7.5	-0.9	0.1	-1.4	-1.2
Mother's working time (No job)							
	Short	-12.0	3.4	0.3	0.4	3.0	-3.4
	Middle	27.6	-1.3	-4.4	0.5	-5.2	-4.7
	Long	-2.0	5.1	-3.2	3.7	-1.6	-7.6
Behavior							
Mouthing activity (no)	Yes	—	4.7	9.0*	3.5	2.5	-0.1
Dirt eating (no)	Yes	—	10.9*	-3.2	9.9	8.9	-11.8
Finger sucking (no)	Sometimes	—	-5.1	8.8†	1.3	0.7	6.6
	Frequently	—	2.4	8.4	7.3	15.6*	16.7*
Environment							
Season (warmer)	Cooler	-4.6	-10.1*	-4.2	-7.5*	-7.9*	-6.2
Father's employment (Non-Port Pirie)							
	Nonsmelter	26.1†	14.9*	17.4†	7.8	19.9†	10.3
	Smelter	52.2†	29.7†	29.4†	21.7†	28.3†	23.1†
Parental smoking (None)							
	One	3.6	5.8	7.4*	5.9	8.2*	4.9
	Both	10.3	9.6	12.3†	9.6*	17.4†	11.0*
Rainwater use							
Cooking (never)	Sometimes	-15.0	-6.2	1.8	-3.2	4.3	-1.2
	Frequently	-4.5	-5.9	0.8	-5.0	2.7	-3.5
Drinking (never)	Sometimes	14.6	7.5	3.0	7.5	-10.2	8.1
	Frequently	13.0	-2.1	-5.4	-3.9	-7.4	-4.6
Soil lead levels (Non-Port Pirie)							
	Lower	5.2	13.0*	2.4	13.0*	7.5	20.8†
	Middle	18.6†	29.3†	13.3†	23.5†	18.4†	24.7†
	Higher	43.3†	47.7†	25.0†	36.3†	32.3†	36.2†

\* $p < .05$ .† $p < .01$ .

results from various mouthing activities during early childhood development. Clinical studies have shown, with certainty, that approximately 40–50% of ingested lead is absorbed from the gastrointestinal tract during early childhood, whereas adults absorb only 5–10% in this manner.<sup>25</sup>

Mean PbBs decreased significantly during ages 2–5 y. This probably was not a consequence of secular changes in the environment because a decrease has been generally observed in many of the studies mentioned; also, there was limited evidence that a cohort effect was operating within Port Pirie when PbB-by-age profiles were constructed for each of the 3 y of recruitment (1979 to 1982). A more feasible explanation is in terms of those factors already invoked to explain the in-

itial rise in PbB, e.g., decreased hand-to-mouth activity (associated with normal child development); this decrease in activity leads to reduced ingestion of lead and/or a decrease in ability over time for the child to absorb ingested lead.

The lack of a difference in mean PbB between preschool girls and boys accords with other studies.<sup>26,27</sup> Divergence of PbBs for boys from girls usually occurs at later ages (6 y to adolescence), and boys consistently record higher values for mean PbB than girls.<sup>22,28</sup> The definite mechanism for this occurrence remains unclear. One explanation is the greater opportunity for boys to ingest lead from their environment because they usually play outside more often than do girls. Moreover, the blood lead measurements were not ad-

justed by packed cell volume in these studies, and the differences could, therefore, be explained in part by the presence of a higher red cell or hemoglobin concentrations in the boys during and after puberty.

The results of analysis indicate that two variables are particularly conspicuous in their association with PbBs. There is a strong, positive gradient in percentage shifts of PbBs relative to local topsoil lead levels. The highest concentrations in PbB have been observed in children who lived in areas with the highest topsoil lead content. This dose-response relationship is evidence for a direct effect of the lead, either in the topsoil or in the air, on body lead burden. It has been predicted elsewhere<sup>29</sup> that the estimated mean natural log-transformed PbB could increase by 0.231  $\mu\text{g}/\text{dl}$  for each unit increase in natural log of the soil lead level.<sup>29</sup> Evidence that lead in household and play yard dust is a major source of childhood body lead burden has been adduced by other observers.<sup>29,30</sup>

Employment of parents at the smelter was another variable significantly associated with higher PbB. Since 1984-1985, employees have been provided with work clothes that do not have to be taken home and with showers. However, these changes occurred too late for their impact on PbBs to become apparent in this study. The persistence of this finding in the multiple regression context suggests that there is no strong confounding with other variables, e.g., place of residence or social status.

There was a positive association between PbB in young children and parental smoking status, a finding that is in agreement with other studies. Sherlock et al.<sup>31</sup> reported higher PbBs in children whose parent(s) smoked, compared with children who resided with nonsmoking parents, although the difference was not statistically significant. Furthermore, in a study of environmental exposure to lead and arsenic among children who lived near a glassworks, there were indications that parental smoking habits had a significant effect on PbB in children.<sup>32</sup> Recently, Willers et al.<sup>33</sup> reported a significant association between higher PbBs in children and parental smoking, and the author ascribed this result to the difference in home environment, family lifestyle, and small airways diseases that affect absorption of inhaled lead particles.

It is difficult to conduct a quantitative assessment of children's behaviors, and the anticipated effects of behavior on PbB have not, therefore, been observed in this study. However, there were some indications that PbBs in children are related to their behaviors, and statistical significance was observed at some ages. The combination of mouthing activities, eating dirt, and sucking fingers supports the study by Charney et al.,<sup>34</sup> who found that a group of 50 children who had high PbBs (40-79  $\mu\text{g}/\text{dl}$ ) played in outside soil, mouthed objects, and sucked their fingers more often than a matched group (PbB,  $\leq 29 \mu\text{g}/\text{dl}$ ).

The mean PbB was influenced by the month in which the children were studied, i.e., peak in PbB during the summer, a finding that has been described by others in nontropical climates.<sup>35</sup> One possible explanation is the seasonal variation in the amount of lead exposure;

most children spend more time playing outside in the summer than in winter, and the rain in winter may stabilize dust.

The significant gradients in mean PbB in relation to mother's education, parental occupation, and use of rain water were no longer statistically significant in multiple regression analysis. This suggests that these variables were at least partially confounded with other factors. For example, the association between the PbB and use of rain water was obviously confounded by residential area. Outside Port Pirie, two-thirds of the children always use rain water for drinking and in prepared foods, whereas one-third of the children used little or no rain water at all. However, the situation was exactly the reverse in Port Pirie.

It is cautioned, however, that the assessment of variation in PbB depends on an understanding of the environmental sources of lead and the means by which lead enters the body. Young children are particularly likely to have many sources of lead exposure from air, food paint, dust, and dirt. The use of a 16-variable model explained 36.3% (at 36 mo) or less (at other ages) of the variation in PbB during early childhood, and other factors associated with changes in PbB almost certainly remain to be identified. Although many of the houses in Port Pirie are more than 50 y old and contain leaded paints, scanning electron microscopy of samples of household dusts<sup>36</sup> revealed that the absolute quantity of paint flakes present in the dust samples was very low and that the total lead levels in the dust were not correlated with measured paint contamination. Moreover, no correlation between lead-based paints and PbBs of children was observed, and Body<sup>36</sup> concluded that unless the individual child exhibited pica, leaded paints were unlikely to contribute to elevated PbBs.<sup>37</sup> Hence, incorporation of paint data in this analysis is unlikely to explain significantly more variation in PbB. Subsequent to the smelter's commissioning of a 205-m stack in 1979 (just prior to the first recruitment of pregnant women for this study), fugitive lead emissions from the smelter have been low.<sup>38</sup> The general level of total suspended particulate lead in Port Pirie was approximately 0.43  $\mu\text{g}/\text{m}^3$  in 1984, which is well below the Australian National Health and Medical Research Council's criterion that "the maximum permissible level of lead in air in the urban environment should be 1.5 micrograms per cubic metre averaged over 3 calendar months." Data on airborne lead were not sufficiently widespread to enable construction of contours of average exposure throughout the residential area for inclusion in this analysis.

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46 **2023510531**

Thacker, S.B., Addiss, D.G., Goodman, R.A., Holloway, B.R., and Spencer, H.C., "Infectious Diseases and Injuries in Child Day Care: Opportunities for Healthier Children," Journal of the American Medical Association 268(13): 1720-1726, 1992.

The authors of this study examined data in order to provide pertinent information on infectious diseases and injuries in child daycare and to outline measures to address these health care needs. The authors reported that "compared with preschool-aged children reared at home, among children in day care the risk of some infectious diseases was two to four times greater." The rates of both intentional and unintentional injuries were somewhat lower for daycare children than for children at home. The authors concluded that "because preschool children spend increasing time in structured day-care settings, the risk for some infectious diseases has increased" and that "at the same time, child day-care settings present opportunities for ensuring healthier children through enhanced development, safer environments, better nutrition, increased vaccination coverage, and health promotion."

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# Infectious Diseases and Injuries in Child Day Care

## Opportunities for Healthier Children

Stephen B. Thacker, MD, MSc; David G. Addiss, MD; Richard A. Goodman, MD  
Barbara R. Holloway, MPH; Harrison C. Spencer, MD

**Objective.**—To provide pertinent background information on infectious diseases and injury in child day care and outline measures to address these health care needs.

**Design.**—We reviewed published English-language literature identified through a MEDLINE bibliographic search, major literature summaries, and bibliographies from identified articles.

**Setting.**—Child day-care settings reviewed included family child care homes, centers, special facilities for ill children, and facilities for children with special needs.

**Patients or Other Participants.**—Primarily children in a variety of day-care settings, often compared with children cared for at home.

**Main Outcomes.**—The occurrence of outbreaks and illness related to infectious disease and injury.

**Results.**—Compared with preschool-aged children reared at home, among children in day care the risk of some infectious diseases was two to four times greater. Rates of both intentional and unintentional injuries in day-care settings were somewhat lower than those for children cared for at home.

**Conclusions.**—Because preschool-aged children spend increasing time in structured day-care settings, the risk for some infectious diseases has increased. At the same time, child day-care settings present opportunities for ensuring healthier children through enhanced development, safer environments, better nutrition, increased vaccination coverage, and health promotion.

(JAMA. 1992;268:1720-1726)

RECENT major social and demographic trends have radically altered the structure and function of families in the United States. These trends include the increasing participation of women in the

paid work force, rising proportions of single-parent families, and more children living in poverty. One consequence of these trends has been a dramatic change in child-rearing arrangements for young children and an intensified need for child day-care services.<sup>1</sup> About 90% of families with preschool children use full- or part-time child day-care services.

As the need for child day-care services has risen, national attention has focused on quantity, availability, and costs associated with these services. At

the same time, however, issues of quality of care—particularly those involving health and safety—have not been addressed adequately. For example, although children can be exposed to unnecessary health or safety risks while in child day care, efforts to develop prevention measures have been constrained by limitations in scientific data on the efficacy, practicality, and cost-effectiveness of alternative strategies.

In this article, we review existing knowledge of two public health issues in child day care—infectious disease and injury. This article provides pertinent background information on infectious diseases and injury in child day care, summarizes basic information about these issues, and outlines measures to address these health needs.

### BACKGROUND

#### Changes in Demographics and Child Day-Care Patterns

In 1988, 60% of children 5 years of age and under (13.3 million children) received child day care.<sup>2</sup> Of these, more than 60% were cared for outside the home, 32.6% in home day care and 31.2% in day-care centers or preschools. More than 80% of the women who work are of childbearing age, and over 90% of these women will become pregnant during the years they are employed outside the home. Since 1970, the proportion of working mothers of children under 5 years of age has risen from approximately 30% to 60%.<sup>1,2</sup> The fastest-growing subgroup of working mothers includes those with

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children under 1 year of age, of whom over 40% are employed.<sup>3</sup> This trend is likely to continue: by the year 2000, more than 75% of mothers with children 5 years of age or under are likely to be working outside the home. Even among children of mothers not currently employed, more than one third had been in a child day-care setting at some time.<sup>2</sup>

Since mothers of preschool-aged children are the fastest-growing segment of the labor force, both the public and private sectors have begun to address the unique work and family issues that concern employers and employees. In particular, the types of child day-care arrangements have proliferated, including those sponsored by corporations, hospitals, and government agencies. The variety of child day-care services now ranges from unregulated in-home child care to licensed child day-care centers (Table 1).<sup>4</sup>

Many companies consider the provision of child-care benefits as an approach to reducing absenteeism and tardiness, decreasing turnover, and enhancing recruitment, morale, and productivity.<sup>5</sup> Employee concerns have increasingly prompted businesses to explore child-care information and referral services, family day care, sick-child care, and before- and after-school programs.

Table 1.—Types of Child Day-Care Settings\*

- Small family child-care home refers to a private family home in which children receive care (including preschool-aged children of the caregiver). Most state licensing codes limit these to a maximum of six children, and usually licensing is not required.
- Large family child-care home usually offers care in a private home serving seven to 12 children (including preschool-aged children of the caregiver) and employs qualified adults. Depending on the state, licensing may or may not be required.
- Centers are licensed facilities, usually caring for 13 or more children for full days or parts of days.
- Special facilities for ill children care only for sick children.
- Facilities for children with special needs usually offer care and education for one or more children with disabilities or chronic illness requiring special surveillance or intervention.

\*Adapted from National Health and Safety Performance Standards: Guidelines for Out-of-Home Child Care Programs.<sup>4</sup>

## Costs of Child Day Care

Child day-care costs continue to escalate and now average \$3000 per child per year (range, \$1500 to \$15 000).<sup>6,7</sup> In the United States, 10% of gross income for a family is expended on child day care; a low-income family may expend up to one third of its gross income on child care.<sup>8</sup> Given these costs, it is not surprising that children with annual family incomes of \$40 000 or more were more likely than children with family incomes less than \$10 000 to ever have received child day care (79% vs 48%).<sup>2</sup>

In addition to costs for routine child day care, each parent may be absent from 1 to 4 weeks annually to care for a sick child.<sup>9-11</sup> Over 60% of employee absenteeism in the workplace may be related to unmet child-care needs, particularly those of sick children; in 1980, 472.1 million days of absenteeism were accounted for by illness or injury.<sup>12</sup> By valuing each day at minimum wage, in 1980, the economic impact of absenteeism associated with illness or injury in a child was \$12.7 billion. Because many employers do not routinely grant leave to care for sick children, employees commonly offer other reasons for absenteeism or may use sick days or vacation days to care for their children.<sup>5</sup> Women report two to three times more hours of work lost than men because of family members' illness.<sup>10,12</sup> At the same time, the availability of child day care enables many parents to work, enhancing family income.<sup>14</sup>

## Methodologic Concerns

The studies summarized in this article are subject to two limitations. First, because child day-care services in the United States are diverse and evolving rapidly, the results may not be generalizable to day care under different regulatory, enforcement, cultural, or social conditions. Second, in day-care settings having routine surveillance, case ascer-

tainment may be enhanced relative to other settings, resulting in inflated risk estimates.

## INFECTIOUS DISEASES IN CHILD DAY CARE

Children who attend day care are at risk for a variety of infectious diseases. For some of these diseases, characteristics of child day-care settings may facilitate transmission of the causative agent(s), increasing the risk that children, members of their households, and day-care staff will become infected. Most of these infectious diseases are mild and self-limiting; however, because they can spread to staff and household members, they may result in loss of work and income. The section below outlines basic considerations regarding the transmission of infectious diseases in child day care, then characterizes these problems in terms of modes of disease transmission.

### Factors Associated With Transmission of Infectious Diseases

At least four host- and environment-related factors contribute to person-to-person or airborne transmission of infectious diseases in child day care:

1. Large numbers of children may be in close and direct physical contact.
2. Infants and young toddlers often have poor personal hygiene, are incontinent of feces, and frequently place their hands and other objects in their mouths.
3. Young children are susceptible to a variety of infectious organisms.
4. With many of the diseases caused by these organisms, infected children may be highly contagious before the onset of symptoms, while other problems (eg, hepatitis A and giardiasis) may not be detected because infected children remain asymptomatic.

The risk of transmission of infectious diseases in child day-care settings also may be increased by suboptimal infection-control practices that reflect limitations in staff capabilities and/or facil-

Table 2.—Evidence for the Association Between Various Diseases Transmitted by the Fecal-Oral Route and Attendance at Day-Care Centers in the United States\*

Disease/Organism	Outbreaks of Illness		Incidence of Illness, per Child-Year	Prevalence of Infection, %	Estimates of Risk Relative to Care at Home
	No.	Attack Rate, %			
Acute diarrhea (unspecified cause)	>100	<10-100	0.4-4.2	...	1.6-3.5
<i>Giardia lamblia</i>	>25	17-54	0.2-0.4†	7.2-26.0	1.8-12.8†
<i>Cryptosporidium</i>	11	17-64	...	0-27	...
<i>Shigella</i>	14	25-73	...	...	Elevated
<i>Salmonella</i>	2	23-70	...	...	...
Hepatitis A	>100	1-8	...	...	Elevated
<i>Escherichia coli</i>	3	34-56	...	...	...
<i>Clostridium difficile</i>	1	32	...	...	...
Rotavirus	15	44-100	0.2-0.6†	12.4	...

\*Among children aged 0 through 36 months. References are available from the authors on request. Ellipses indicate data not available.

†Refers to infection rather than illness.

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ities. For example, many day-care centers are not equipped or staffed to care effectively for mildly ill children. These constraints may be compounded by understaffing, low pay for child-care providers, high rates of staff turnover, and lack of adequate training in infection control.

### Characterizing the Occurrence of Infectious Diseases

In this section, characterization of the occurrence of infectious diseases in child day care is based on information and data reported from a variety of sources. For example, investigations of outbreaks in child day-care settings have documented the occurrence of some infectious diseases, while descriptive and long-term epidemiologic studies in these settings have provided estimates of the incidence or prevalence of certain diseases. In general, however, these studies have not established estimates of the relative frequency or risk of infectious diseases among children in day care compared with children cared for at home. Such estimates have been provided by community-based comparative studies using case-control, cross-sectional, or prospective methodologies. Although these studies have been limited in scope and design, they have provided the most useful data on risk of infection or disease in day-care centers in comparison with other child-care settings.

In this summary, infectious diseases in child day care are grouped by three principal modes of transmission: (1) person-to-person spread by the fecal-oral route; (2) person-to-person spread by contact with skin, excretions, or bodily fluids; and (3) transmission by aerosols or respiratory droplets. In the United States, few common-source food-borne or waterborne outbreaks have been documented in child day care.

#### Person-to-Person Spread

**Fecal-Oral Transmission.**—Infectious agents transmitted by the fecal-oral route have caused cases of both sporadic and outbreak-related illness in day-care settings. These agents include parasites (eg, *Giardia lamblia* and *Cryptosporidium* species), bacteria (eg, *Shigella*, *Salmonella*, and *Campylobacter* species and *Escherichia coli*), and viruses (eg, hepatitis A virus and rotavirus).<sup>15,16</sup> Reports published since the 1970s have helped to characterize the impact of these agents in outbreaks occurring in child day care and to compare the occurrence of the most common enteric infections among children in day care with the occurrence among children cared for at home.

Data from studies in Houston, Tex,

indicate that an average of 1.4 to 3.0 outbreaks of diarrhea occur in day-care centers each year.<sup>15,17</sup> Among children attending day care, the estimated incidence of diarrhea ranges from 0.4 to 4.2 episodes per child-year (Table 2).<sup>18-21</sup> Comparative studies indicate that this risk is approximately 1.6 to 3.5 times higher than for children who receive care at home.<sup>20,22,23</sup> However, for children who are cared for in homes other than their own, this risk is nearly equal to that of children cared for at home. For some agents (eg, *Shigella* and *Giardia* species and hepatitis A virus), secondary spread occurs commonly to household members and community contacts of children who attend day care.<sup>24-28</sup>

At least three conditions increase the risk for diarrheal illness among children attending day-care centers. First, children are at greatest risk just after admission to a day-care center.<sup>21,29</sup> Second, diarrheal illness may be more common in centers that care for children who are not toilet-trained or who are less than 2 years of age. Third, children may be at increased risk if they attend a day-care facility in which the same staff person both changes diapers and prepares meals or where diapering or hand-washing practices are not optimal. In contrast, findings from previous studies are inconsistent regarding the role of center size or the gender of the child as a risk factor for diarrhea.

Outbreaks of hepatitis A in day-care centers have been well documented and occur more frequently in centers that are large, provide care to children less than 2 years of age, and are open for longer hours.<sup>28</sup> After hepatitis A virus has been introduced, the risk of transmission within the day-care center increases in relation to the number of children wearing diapers and the degree of mixing between groups of different ages. Substantial transmission outside the day-care environment (eg, to parents) may occur and may account for 70% to 80% of cases.<sup>25</sup> National surveillance data, prospective studies, and outbreak investigations indicate that the risk of acquiring hepatitis A infection appears to be greater for children attending day-care centers; however, there have been no well-controlled comparative studies to quantify the magnitude of this risk.

Hand washing is probably the single most important measure for the prevention of illness caused by enteric pathogens. For example, in day-care centers that have implemented a hand-washing training program, rates of diarrheal illness have declined by 50%<sup>30</sup>, even more important than training, however, is the need for effective monitor-

ing and enforcement of good hand-washing practices.<sup>31</sup> Frequent cleaning and disinfection of surfaces and toys may also be important for some infectious agents, such as hepatitis A virus.

Although transmission of enteric pathogens to other children in the day-care center may be prevented by excluding attendees who have uncontrolled diarrhea, this approach has not been fully evaluated. Moreover, when strict exclusion criteria are enforced in one center, an ill child may be taken to another center with less strict criteria, propagating transmission within the community. Alternatively, reports from some outbreak investigations show that isolation of an affected child (or cohorting of affected children) may limit transmission within the center.<sup>24,32</sup> Prevention of hepatitis A infection requires an additional measure—the prompt administration of immune globulin to those who have had contact with infected children. Finally, the asymptomatic occurrence of many enteric infections (eg, hepatitis A and *Giardia*) among young children complicates the prevention of transmission of agents by the fecal-oral route and underscores the importance of rigorous hand-washing practices in child day-care settings.

**Excretions, Body Fluids, and Skin.**—**Cytomegalovirus.**—In child day-care settings, cytomegalovirus may be transmitted by direct contact from infected children to susceptible persons, including day-care providers, by infective secretions (primarily urine and saliva).<sup>33,34</sup> The pathogenicity of cytomegalovirus infection is limited among healthy children and adults, and infection with cytomegalovirus is usually asymptomatic. However, in utero transmission can occur, and cytomegalovirus infection can produce serious sequelae. Therefore, the implications of exposure to cytomegalovirus are greatest for women who are pregnant and providing day care to infected children.<sup>34</sup> At present, hand washing—as a general hygienic practice—is the only specific measure that can be recommended for prevention of cytomegalovirus infection in child day care.

**Hepatitis B Virus.**—Although person-to-person transmission of hepatitis B virus has been documented in some situations of close personal contact, public health surveillance data and epidemiologic investigations suggest that transmission of hepatitis B virus is possible but rare in child day-care settings.<sup>28,35</sup> In particular, the findings in an investigation of one case of acute hepatitis B involving a child attending a day-care center in the United States suggested that infection was associated with being bitten by another child who was a long-

Table 3.—Studies of the Occurrence of Injury in Child Day-Care Centers in the United States, 1964-1989

Source, y	Location	Design	No. of Centers	No. of Children	Ages	Socioeconomic Status	Injuries*			
							Total No.	Rate per Child per Year	Seeing Physicians	
									No.	Rate per 1000 Children per Year
Center-Based Studies										
Bitner and DeLissovoy, <sup>52</sup> 1964	Hershey, Pa	Record review	1	58	3-4 y	Middle	173	5.1	NA	NA
Solomons et al., <sup>53</sup> 1982	Iowa City	Record review	1	133	2 mo-6 y	Middle	488	0.7	6	9.0
Elardo et al., <sup>54</sup> 1987	Iowa City	Record review	1	133	2 mo-6 y	Middle	1324	2.8	4	8.6
Lee and Bass, <sup>55</sup> 1990	Los Angeles, Calif	Record review	1	400	0-6+ y	Middle	103	0.3	2	5.0
Population-Based Studies										
Landman and Landman, <sup>56</sup> 1987	Maryland	Telephone survey	431	18 728	2-5 y	Mixed	29	0.1	18	70.2
Rivara et al., <sup>59</sup> 1989	Puget Sound, Wash	Daily record review	NA	2204	0-4 y	Middle	NA	NA	384	173.0
Chang et al., <sup>57</sup> 1989	Los Angeles	Record review	90	21 435	2-5 y	Low	423	0.02	54	2.5
Sacks et al., <sup>58</sup> 1989	Atlanta, Ga	Prospective	71	5390	0-12 y	Mixed	NA	NA	143	27.0

\*Injuries are defined differently in the various studies, accounting for some of the variations in rates. NA indicates information not available.

term carrier of the hepatitis B virus.<sup>33</sup> Recommendations for preventing the transmission of hepatitis B virus in day-care centers focus on exposures to contaminated blood or body fluids but also address the needs for educating staff, for hand washing, and for applying appropriate environmental measures.<sup>35</sup>

**Human Immunodeficiency Virus.**—On the basis of knowledge of the epidemiology of hepatitis B infection, there is a theoretical risk for transmission of human immunodeficiency virus in child day-care settings—specifically, through exposure to contaminated blood or blood-containing fluids.<sup>36,37</sup> However, the level of this risk is considered to be extremely low, and there is no evidence for transmission of human immunodeficiency virus in this setting.<sup>37</sup>

Specific recommendations have been developed regarding the admission to child day care of children infected with human immunodeficiency virus.<sup>37</sup> Other than routine precautions for handling blood and blood-containing body fluids, however, no specific measures have been recommended.<sup>37</sup>

**Skin Contact: Lice, Scabies, Ringworm, and Impetigo.**—The potential for cutaneous infestations and skin infections in the child day-care setting is suggested by the close contact between children and by reports of such outbreaks among schoolchildren.<sup>38</sup> However, these problems have not been documented extensively in the biomedical literature.

#### Transmission by Aerosols or Respiratory Droplets

**Acute Upper-Respiratory-Tract Illness.**—This syndrome is the most common medical problem among children attending day-care centers. By age 2 years, children attending day-care centers have an estimated seven or eight

episodes of acute respiratory illness per year,<sup>39,40</sup> an incidence up to 1.6 times greater than among children not attending day-care centers.<sup>39-41</sup> However, the magnitude of this difference is inversely related to duration of time in day care, and the total number of episodes of respiratory illness in preschool-aged children appears to be independent of day-care center attendance.<sup>39,42,43</sup> Therefore, children less than age 2 years who attend day-care centers are more likely to acquire respiratory infections at an earlier age than those cared for at home. The degree to which earlier exposure to respiratory pathogens increases the risk of complications and sequelae (e.g., chronic otitis media and hearing loss) is unclear.

Because a broad range of respiratory pathogens may be transmitted in child day-care settings, the epidemiology of problems associated with respiratory or aerosol spread routes are less clearly defined than for pathogens transmitted by the fecal-oral route. However, several respiratory viruses (in particular, respiratory syncytial virus, parainfluenza, adenovirus, enterovirus, and rhinovirus) occur commonly in the child day-care setting and together may account for nearly one third of all respiratory illness in day-care centers.<sup>44</sup>

Nasopharyngeal carriage of bacterial pathogens may be more common in day-care centers than in other settings; three of these (ie, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and group A *Streptococcus*) have been isolated from 22% to 52% of day-care center attendees with respiratory illness.<sup>45</sup> In addition, outbreaks of tuberculosis have been reported in at least two family day-care homes.<sup>46,47</sup>

Data regarding the comparative risks of some vaccine-preventable diseases (ie,

measles, mumps, pertussis, and rubella) among children attending day care and those participating in other types of child-care arrangements are limited. Although transmission within day-care centers has contributed to sustained outbreaks of measles, day-care centers have been considered the primary setting of measles outbreaks in only 1% of cases in the United States.<sup>48</sup> In most states, because state regulations require vaccination of attendees of licensed day-care centers, percentages of children vaccinated are generally higher for those children than for children not in licensed day care.

Because many children and adults with respiratory illness may be infectious before the onset of symptoms, prevention of these problems in child day-care settings is difficult. Moreover, even though aerosols and respiratory droplets are the major modes of spread, fomites and person-to-person contact may contribute to transmission of respiratory pathogens. Because of these considerations, most factors associated with the occurrence of acute respiratory illness in child day care cannot be modified substantially. Hand washing and regular disinfection of toys and other possible fomites are two potential measures for reducing transmission of respiratory pathogens in the child day-care environment. In addition, ensuring that all children are vaccinated against vaccine-preventable diseases is essential. The importance of this strategy may also increase as additional vaccines against other respiratory pathogens are developed. Finally, the resurgence of tuberculosis in certain areas underscores the need for child day-care and health-care providers to be knowledgeable about the need for screening in high-risk populations.

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**Otitis Media.**—In the United States and other industrialized countries, acute otitis media affecting children is a common problem following acute upper-respiratory-tract infections. Epidemiologic and clinical studies have increasingly suggested that children attending day care are at greater risk for acute otitis media than children in home care.<sup>45,49</sup>

In general, otitis media results as a bacterial complication of antecedent upper-respiratory-tract viral infections; the most commonly implicated bacterial pathogens include *S pneumoniae* and nontypeable *H influenzae*. Efforts to develop agent-specific vaccines offer some prospects for prevention of otitis media in the future. However, current options are limited and rely on fundamental infection-control measures, including hand washing and basic environmental hygiene.

**Meningitis.**—Although many children may be nasopharyngeal carriers of *H influenzae* type b, the risks of meningitis and other invasive clinical diseases in these children have not been clearly established. However, attendance at organized day care is considered to be a risk factor for primary invasive *H influenzae* type b disease<sup>50</sup>; this risk is inversely proportionate to age and is highest for children less than age 2 years, probably reflecting increased exposure to infectious respiratory secretions. Less clear is whether day-care attendance is associated with an increased risk for secondary *H influenzae* type b disease. *Neisseria meningitidis* also causes meningitis in the day-care setting, but the risk associated with attendance at day care is unknown.

The recent availability of effective *H influenzae* type b conjugate vaccines offers prospects for dramatically reducing the overall occurrence of meningitis and other invasive *H influenzae* type b disease as well as the occurrence of these problems in child day care.<sup>51</sup> Accordingly, efforts to prevent primary invasive *H influenzae* type b disease should be directed toward implementing the recommendation that all children receive one of the conjugate vaccines licensed for infant use beginning routinely at age 2 months.<sup>51</sup>

#### INJURY IN CHILD DAY CARE

Methods used to characterize the epidemiology of injury in child day care have included studies focused on individual day-care centers, population-based studies, prospective studies, ongoing surveillance, and studies of case series and registries. The section below summarizes data regarding the epidemiology of and risk factors for both in-

tentional and unintentional injury in child day care.

#### Injury Occurrence

Rates of injury in child day care vary in relation to several factors, including location, demographics, type of child care, definition of injury, data sources, and study design. One approach to estimating the risk of injury has been to focus on individual child day-care settings. In four such studies involving record reviews of university-based child day care,<sup>52-55</sup> annual injury rates ranged from 0.7 to 5.1 injuries per child (Table 3). In one day-care center, during a 42-month period, almost 90% of attendees were involved in incidents that were judged by the staff to require documentation<sup>54</sup>; virtually all of these injuries involved either the head (73%) or limbs (23%), and 96% of the injured children were treated adequately by washing, application of ice, and attention from adults. In general, the most common injuries were abrasions and swellings involving the head and limbs, usually secondary to falls.

Population-based estimates of the risk of injury have been derived from telephone surveys, record reviews, and prospective case ascertainment (Table 3).<sup>56-59</sup> In addition to estimating risk of occurrence, these studies have provided estimates of the need for medical evaluation. For example, a telephone survey in Maryland suggested that 7% of children in day care required medical attention for injuries and that 4% required activity restriction because of the injuries.<sup>56</sup>

Rates of injury for children in day care are somewhat lower than those for children in the general population. Among a group of 1199 children less than age 5 years enrolled in a health maintenance organization, prospective monitoring indicated that the rate of injuries in day care was 2.5 per 100 000 child-hours of exposure compared with 4.9 per 100 000 child-hours of exposure in the home environment.<sup>59</sup> A national telephone survey regarding health events in child day care found a rate of injury during child day care of 1.7 per 100 000 child-hours of exposure compared with 2.7 per 100 000 child-hours of exposure at home.<sup>60</sup>

Rates of injury in child day care vary by age, although the age of highest incidence varies among studies.<sup>52,53,55,57-59</sup> Rates of injury peak at about 11 AM and again at 4 PM and vary by season, with the highest rates occurring in summer and spring; seasonal rates have also varied by age of the child. The playground was the most frequent site of injury.<sup>54,56-58</sup>

Human bites are an underrecognized problem associated with the congregation of large numbers of preschool-aged children in child day care.<sup>61,62</sup> For example, in one retrospective cohort study, 104 (46%) of 224 children enrolled in a day-care center for 1 or more days during a 12-month period incurred at least one human bite.<sup>61</sup> In this day-care center—which served a white, middle-class population—a male toddler was likely to be bitten nine times if enrolled full-time. The risk for being bitten was increased during the middle of the morning and in September, the opening month for a center operating only during the school year. In the absence of comparative data from children in other settings, however, the relative risk of bite injuries is not clear.

#### Child Abuse

Although a theoretical basis for maltreatment of children by staff has been suggested,<sup>63</sup> epidemiologic data regarding intentional injury (caused by staff or children) in day-care settings are limited. For example, in 1985-1986, 6005 reports of physical abuse and 2372 cases of sexual abuse were confirmed statewide in the Iowa Child Abuse Registry<sup>64</sup>; of these, only two reports involved child day-care centers. However, other reports have indicated the occurrence of physical and sexual abuse that requires appropriate clinical and supportive intervention.<sup>65,66</sup>

In North Carolina, the complaint log maintained by the Office of Child Day Care Licensing recorded 424 complaints during the year ending in mid-1988.<sup>67</sup> Although most complaints related to licensing (45%) or to violations of basic standards, such as staff-child ratios (39%), approximately 17% were allegations of abuse or neglect (of which fewer than one third led to "strong" interventions). Complaints against unregistered homes were three times as likely to be judged severe as those against registered homes, and day-care centers meeting only minimum licensing standards were five times more likely to have a severe complaint than those meeting higher standards.

Potential cases of sexual abuse associated with child day care were identified through a survey of licensing and child-protection officials in all 50 states, through contact with 48 clinicians specializing in sexual abuse, and through a search of newspaper articles.<sup>68</sup> For the 3-year period ending in December 1985, 1639 victimized children were identified in 270 facilities. Adjusting for missing data, the authors estimated an annual rate of 5.5 sexually abused children per 10 000 enrolled in day-care centers (not

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family day-care homes), a rate lower than national figures of 8.9 per 10 000 for children less than age 6 years in families.<sup>68</sup> Most cases (83%) involved a single perpetrator in an isolated setting, such as a bathroom; the perpetrator was a child-care worker in 62% of cases and was usually a man (60%). In half the instances there was a single victim, usually a girl (62%). No useful predictors were found to identify perpetrators, victims, or centers. Indeed, usual indicators of day-care quality were not associated with low risk, although facilities where parents had ready access to their children were less likely to have cases of sexual abuse.

### Prevention

The occurrence of injury among children in day-care settings underscores the opportunities and needs for specific measures to prevent this problem. Because playgrounds are common sites for injuries,<sup>34,56,57</sup> preventive efforts have focused on playground apparatus and, in particular, impact-absorbing surfaces under climbing equipment.<sup>69-71</sup> One study of injury hazards in home day-care facilities indicated that 29% of indoor and playground items were unsafe.<sup>72</sup> In particular, knives and other sharp objects were accessible to children in the kitchens in 69% of homes, cleaning supplies in 35%, and hot-water temperatures in excess of 49°C in 69%. Moreover, 89% of outdoor playgrounds had climbing equipment without energy-absorbing material underneath.

These findings are a reminder that playground-related injuries can be addressed effectively through methods such as the exclusion of high-risk apparatus (eg, climbers), installation of impact-absorbing surfaces, and increased supervision at times of highest risk. Investigators in a study of 66 Atlanta child day-care centers demonstrated that the risk of injury was proportionate to the number of playground hazards and recommended the development and enforcement of effective regulation of playground equipment at these centers.<sup>73</sup> Educational efforts to significantly reduce hazards in these settings, however, have had limited success.<sup>74</sup>

In general, parents in the United States are not well informed about risks of injury to their children who attend day care; parents of lower economic status are particularly poorly informed.<sup>75</sup> Moreover, even well-educated employees of one health care institution tolerated unsafe features in day-care centers,<sup>76</sup> and only 11% of these parents considered safety when choosing a day-care facility.

Child day care is an excellent and ef-

ficient opportunity for educating children and providers about the prevention of intentional and unintentional injuries, not only in day-care settings but also in the home. For example, an educational curriculum for increasing safety-seat and seat-belt use in preschool programs in Los Angeles, Calif. increased the use of safety restraints from 22% to 44% two weeks after the curriculum was completed, while no change occurred in programs without the curriculum.<sup>77</sup> A subsequent decrease in the use of safety restraints suggested the need for continuing educational reinforcement. Evaluation of a program to train child day-care personnel in addressing child abuse suggested that a special training course had minimal impact on staff participation in intervention activities or on the development of adequate written policies for the management of child abuse.<sup>78</sup> However, programs with personnel receiving special training were more likely to be involved in prevention activities to utilize community referral resources for high-risk families.

### COMMENT

Since the early 1970s, dramatic social and economic changes have led to the emergence of child day care as an integral component of the social fabric in the United States, with major implications for the practice of medicine. Because children are spending substantially more time in structured settings with other children, their risk for many infectious diseases has increased. On the other hand, child day-care settings represent opportunities for ensuring healthier children in the United States through enhanced development, safer environment, better nutrition, increased coverage with vaccination, and health promotion.

Physicians and other health care professionals should join with parents, public health organizations, and others at the forefront of a reasoned and rapid national response to the changes brought on by child day care. The recent publication of the health and safety standards developed jointly by the American Academy of Pediatrics and the American Public Health Association was an important early step in addressing this need.<sup>4</sup> Primary care providers—especially pediatricians and family physicians—must recognize not only the health and safety issues related to child day care but also their critical role and the impact of child day care on child development (cognitive and behavioral).<sup>79</sup> Members of racial and ethnic minorities or children with special needs, such as those with disabilities, may require particular attention in regard to day-care needs. Physicians who provide care to adults must

be sensitive to the health impact of child day care on day-care workers, who are at higher risk of infectious diseases, and parents, who are subject to stress from the dual responsibilities of work and parenting.

Finally, clinicians and public health departments play a critical role in the assurance of quality in child-care settings through disease and injury control and by health promotion through training and education of parents, staff, and children.

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Krzyzanowski, M., Quackenboss, J.J., and Lebowitz, M.D., "Relation of Peak Expiratory Flow Rates and Symptoms to Ambient Ozone," Arch Environ Health 47(2): 107-115, 1992.

The authors studied the temporal association between peak expiratory flow rates (PEFRs) and ambient ozone in a group of 287 children and 523 nonsmoking adults. The authors reported that "in general, the respiratory response to low-level ambient O<sub>3</sub> is acute, occurs more in asthmatics, and increases as temperature and PM<sub>10</sub> increase." The authors controlled for SES, crowding, cigarette smoke exposure, gas stoves, and actual monitoring results. Adjustment for ETS exposure did not change the results of the analysis.

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## Relation of Peak Expiratory Flow Rates and Symptoms to Ambient Ozone

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**ABSTRACT.** The temporal association between peak expiratory flow rates (PEFRs) and ambient ozone ( $O_3$ ) was studied in a group of 287 children and 523 nonsmoking adults in Tucson. In children, noon PEFRs were decreased on days when there was a higher  $O_3$  concentration; children with physician-confirmed asthma experienced the greatest decrease in noon PEFR. Evening PEFR levels were also significantly related to  $O_3$  in children, especially asthmatics. Among adults, evening PEFRs were decreased in asthmatics who spent more time outdoors on days when  $O_3$  levels were higher. After we adjusted for covariates, significant effects of interactions of 8-h  $O_3$  levels with particulate matter ( $PM_{10}$ ) and temperature on daily PEFR were found. There was some overnight effect of 8-h  $O_3$  on morning PEFRs. In general, the respiratory response to low-level ambient  $O_3$  is acute, occurs more in asthmatics, and increases as temperature and  $PM_{10}$  increase.

SHORT-TERM lung function declines that result from exposure to relatively low concentrations of ozone ( $O_3$ ) have been reported in many studies,<sup>1-16</sup> and these declines have been reviewed very recently by Lippmann.<sup>1</sup> Most of the evidence is derived from exposure chamber studies,<sup>7-9,11</sup> in which changes have been observed in subjects who are exposed to  $O_3$  concentrations that range from 120 to 180 ppb for 1- to 3-h periods. Studies of children who attend summer camps,<sup>2,3</sup> of school-age

children,<sup>4</sup> and of children and adolescents in Tucson<sup>5</sup> have reported associations between lung function and ambient  $O_3$  (1-h maximum concentrations below 120 ppb). A correlation of lung function with ambient  $O_3$  exposure has been reported in a few adult studies.<sup>5,6</sup> Recent laboratory experiments in which  $O_3$  exposure lasted 6.6 h<sup>7,8</sup> indicate that duration of exposure is an important factor in producing a response. Therefore, the health effects of relatively low  $O_3$  levels that persist

for several hours in an atmosphere<sup>9</sup> may be more pronounced than expected, based on the measured 1-h maximum O<sub>3</sub> concentration. Also, a cumulative effect of O<sub>3</sub> concentration that was elevated during a few consecutive days was suggested by the summer camp data.<sup>10</sup>

In this study, we analyzed the relationship of peak expiratory flow rates (PEFRs) to ambient O<sub>3</sub> concentration. The latter was estimated as (a) the daily 1-h maximum and the 8-h maximum moving average and (b) the 8-h average maximum from values obtained on preceding days, including the mean of these values for the previous 4 d. In this study period, the maximum ambient O<sub>3</sub> concentrations were relatively low, i.e., the 1-h maximum never exceeded 92 ppb. Daily variations of PEFRs and symptoms were evaluated, and PEFRs of children and nonsmoking adults were examined. The subjects were from a community population in Tucson.

The purpose of this study was to evaluate the temporal pattern of lung function response to O<sub>3</sub> exposure. Specific aims were to estimate if (a) detectable PEFR changes in real-life situations are related to short-term or to prolonged exposure, (b) if the changes persist overnight, and (c) if there is a cumulative effect of the exposure that lasts a few consecutive days. Furthermore, we evaluated possible differences in these responses that were attributable to asthma or other respiratory diseases. Also, we evaluated O<sub>3</sub> interactions with additional exposures to passive smoking to outdoor particulate matter and/or to outdoor temperature. In response to the question of possible seasonal adaptation to the exposure,<sup>11</sup> we tested to determine if responses to O<sub>3</sub> exposure in spring were greater than in other seasons.

## Methods

The detailed description of the study population and methods of data collection have been presented previously.<sup>12</sup> Briefly, the population for this study was derived from the municipal employees of the local county government and their families. This population included a wide spectrum of socioeconomic status (SES) and was representative of SES within the employed population in this geographic area. It also had fairly representative distributions of age, sex, and ethnic groups. Information gleaned during the initial screening with questionnaires was used to select a sample of households. It was important to include a sufficient number of children in the sample; therefore, only the households with children 5–15 y of age were eligible for this study. The peak flow measurements analyzed in this study were collected during 2-wk periods, from May 1986 through November 1988, and a fairly uniform distribution of subjects was studied in each season.

Basic individual characteristics were determined from modified standard health questionnaires<sup>13</sup>; additional sections were included that identified normal activity patterns and symptomatic responses to environmental factors. Adults completed the questionnaires for themselves and for their children. Peak expiratory flow rates were measured with mini-Wright peak flow me-

ters, a description and discussion of which has been presented previously.<sup>5,14,17</sup> Tests were performed during four or fewer time periods each day: (1) morning (on rising), (2) near noon, (3) evening (4–7 P.M.), and (4) prior to going to bed. Each subject was trained to use the peak flow meter, and they were requested to perform three tests for each time period (morning, noon, evening, bed) and to record the largest value in their diary. Children's tests were supervised by an adult, who also recorded the results. Only one peak flow meter was assigned to each household. This prevented measurement at noon for many of the family members who were away from their homes at noon. We sought to eliminate a possible learning effect; therefore, data were eliminated from the initial 2 d of observation (which demonstrated improvement), thus limiting the observation period to 12 d. In this analysis, we used the data from the morning, noon, and evening measurements only. Daily diaries were also used to record symptoms, medication usage, and activity patterns, in a manner used and described previously.<sup>5,12,17</sup>

Outdoor data for O<sub>3</sub> were obtained from the Pima County Department of Environmental Quality (PCDEQ). An EPA-sponsored inventory of O<sub>3</sub> in the basin produced quite uniform values, which accords with what has been reported previously.<sup>6</sup> Therefore, it was not deemed necessary to include more than three monitoring locations in the basin to guarantee accurate outdoor exposure estimates. The hourly averages from the PCDEQ chemiluminescent monitors were obtained on tape. These files were processed to identify the O<sub>3</sub> records for each study day and to determine the maximum 1-h concentration and the maximum 8-h moving average of 1-h values for each location. Stations for which more than 3 h of O<sub>3</sub> measurements were missing between 9 A.M. and 7 P.M. were excluded from the analysis for that day. The 8-h moving average was not calculated if more than 2 hr of measurements were missing from that 8-h period. The maximum concentrations differed slightly among the monitoring stations, but the correlation of the measurements was very high (correlation coefficient between 0.64 and 0.91 for each pair of the stations for 1-h and 8-h maxima). Thus, the maximum 1-h and 8-h average values from the three stations were used to represent the O<sub>3</sub> concentrations for all subjects who were studied on a given day. For each day of the study, the mean of the maximum 8-h average O<sub>3</sub> concentrations for the 4 preceding days was calculated to be an index of cumulative exposure. Because indoor O<sub>3</sub> concentrations were between 0 and 0.035 ppm,<sup>5</sup> as determined by the use of identical Dasibi monitors as were used outdoors, O<sub>3</sub> exposure was based on outdoor levels, which were adjusted for time outdoors.

During part of the study period, data regarding ambient concentrations of particulate matter (less than 10  $\mu$ m diameter [PM<sub>10</sub>]) were collected daily at one monitoring station, and the data were used in the analysis.

The relationship of PEFR values to O<sub>3</sub> levels was analyzed with two statistical models. A second statistical model was used to account for the evident autocorrelation of PEFR measurements in each subject (relative to

O<sub>3</sub>). In this version of the random-effects longitudinal model,<sup>18,19</sup> the within-subjects' observations include a first-order autoregressive serial correlation component and random observational errors. This model can be applied to data collected by an unequal number of observations per subject, which can be accomplished at unequal intervals. Examination of PEFR measurements indicated that there was no systematic trend in the daily PEFR values of each subject during the 12-d observation period (after data from the 2 initial days were excluded). Thus, the within-subject (random) effect was constant, and we have modeled the effects of O<sub>3</sub> and other covariables as population parameters. The model allows inclusion of both fixed and time-dependent covariates. In this analysis, the constant covariates were gender (1 = female, 0 = male); age; subject-reported asthma status (1 = current disease diagnosed by a doctor, other = 0); exposure to environmental tobacco smoke (ETS = 1 if there was any smoking in the household during the week of PEFR measurements, 0 if no smoking); work in dusty jobs or exposure to gases or fumes at work during the past year (yes = 1, no = 0); and spring season (March = 1, otherwise = 0). The time-dependent covariates were O<sub>3</sub> concentration; time spent outdoors during the day; maximum outdoor temperature; presence of acute respiratory illness or symptoms during the day (sore throat, cough, wheezing or whistling in the chest, shortness of breath with wheezing, chest tightness [ARI = 1 if yes]); and PM<sub>10</sub> concentration. Among the time-dependent covariates, there were also the indicator (0, 1) variables that corresponded to time of the day when the PEFR measurement was taken. The main effects of these variables represented the natural diurnal variability of PEFR values.<sup>17,20,21</sup> Interactions of these variables with other factors indicate the additional effect of the factor on the PEFR measured at a given time of day (e.g., the term "O<sub>3</sub> \* evening" corresponds to the change in evening PEFR measurement that results from a unit change in O<sub>3</sub> concentration). The interaction of an indicator (0, 1) variable with O<sub>3</sub> corresponds to the additional effect when the factor is present (e.g., the term "O<sub>3</sub> \* asthma" reflects an additional change in PEFR that results from O<sub>3</sub> in asthmatics). Interaction terms were evaluated with all respective main effects included in the model. In cases where the elimination of a nonsignificant main effect did not affect the value of the coefficient that corresponded to the interaction term, the main effect was removed from the final model. This would occur when an effect was limited to a subgroup of the population, and all other subjects were included in a reference group.

The analysis was performed separately for subjects who were aged 6–15 y and for those who were more than 15 y of age. We also studied separately the effects of O<sub>3</sub>, which were estimated as the maximum 1-h and 8-h mean values. This was done to limit the number of factors in a single model and to avoid the consideration of co-linear factors in one model (the correlation of 1-h and 8-h values was 0.88). Several different random effects models were tested (fitted to the data), which assured selection of the models that best described the

relationship of PEFR to O<sub>3</sub> concentration and its interactions with other factors (accounting for significant confounding effects). The significance of terms of the models (i.e., model parameters) was tested by the log-likelihood ratio test; the significance level was  $p < .05$ , and  $p$  values between .05 and .10 were considered to be borderline significant. We present the "best" parsimonious models. The terms absent in the models presented were found to be nonsignificant ( $p > .10$ ) or did not modify the relationship between PEFR and O<sub>3</sub>.

A second statistical method, multifactorial analysis of covariance (ANCOVA),<sup>5</sup> was used to analyze day-to-day changes in daily average PEFRs and symptom prevalence rates (the dependent variables) in relation to 8-h O<sub>3</sub> values on the same and previous days (lags of 0 and 1). For this purpose, we used data from 1 007 days of observation, compiled from the 2-wk test periods, for all subjects. Mean daily averages were calculated specifically for morning and evening PEFRs. The distributions of daily symptom prevalence rates were skewed; therefore, log transforms of the rates were used as dependent variables. Demographic and social confounding or covariables included the mean number of hours spent outdoors and the proportions of the population on each day that were in each of the following categories: male, under age 15 y, lived in households (HH) where the head of HH obtained less than a high-school education (SES), smoked, exposed to environmental tobacco smoke (ETS) or to gas cooking in the home, worked away from home or were at school, and worked in jobs with dust or fume exposures. Nitrogen dioxide, PM<sub>10</sub>, and weather measurements were also used as co- or confounding variables. Meteorological covariables included season, daily maximum and minimum temperatures, average wind speed, and average dew point. The ANCOVA yielded adjusted values, expressed changes from the grand mean of the dependent variable (e.g., PEFR), for explanatory variables as independent effects (adjusted for each other and for covariables), and for interactions (adjusted for all other variables).

## Results

The peak expiratory flow values were measured in 287 children (mean age = 10.4 y) and 523 adult non-smokers (mean age = 40.1), for whom acceptable O<sub>3</sub> concentration data had been collected at least 1 d. In both groups, the proportion of males was similar (53% and 54%, respectively). The proportion of children who lived in homes inhabited by smokers was higher than the proportion who lived with adult nonsmokers (44% versus 33%, respectively). More children than adults reported a current asthma condition diagnosed by a doctor (13% versus 9%, respectively). Acute respiratory illnesses and symptoms were recorded for 15% and 14% of the person-days among children and adults, respectively. Children reported that they remained outdoors an average of 2.9 h per person-day, and adults reported 2.7 h per person-day. The mean maximal daily outdoor temperature was 87 °F (30 °C) per person-day. The maximum level of PM<sub>10</sub>, recorded

during the study days, was  $187 \mu\text{g}/\text{m}^3$  (mean =  $42 \mu\text{g}/\text{m}^3$ ).

During the study period (i.e., during collection of the PEFR data), the  $\text{O}_3$  maximum 1-h concentrations ranged from 15 to 92 ppb (mean  $\pm$  standard deviation =  $55 \pm 14$  ppb). Moving average maximum 8-h concentrations ranged from 9 to 82 ppb ( $46 \pm 13$  ppb [Fig. 1]). The highest concentrations of  $\text{O}_3$  were usually attained by noon on each day and persisted for several hours. On many days, sharp declines in  $\text{O}_3$  levels were noted only after 6 P.M.

**Results of random effects models.** Data for at least 6 d, during which at least 12 observations were made, were available for 78% of the children. All children combined provided 5 483 observations. Separate models were used for adults so that the effects of  $\text{O}_3$  on evening and on noon PEFR levels could be evaluated. Morning or evening data for at least 6 d (12 or more data points) were available for 74% of the adults. There were 8 122 morning or evening PEFR measurements for all adults. Noon measurements were missing more frequently than measurements performed at other times of the day. Personal PEF meters were available for only 50% of person-days, and PEFR values were measured in the morning and evening, thus yielding only 6 852 paired observations to use for the estimation of effects of  $\text{O}_3$  on noon PEFR levels in adults.

The estimated effects of  $\text{O}_3$  on PEFRs are presented in Tables 1 (children) and 2 (adults). In all models, there were significant effects of the time of day when PEFR measurements were performed, which reflected a natural increase in PEFR during the day, followed by its overnight decline. In both children and adults who had currently diagnosed asthma, the diurnal variability of PEFRs was significantly greater, and the morning levels were usually lower than levels found in nonasthmatics.

The noon PEFR levels in children were lower on days with higher 1-h maximum  $\text{O}_3$  levels (Table 1, Model I). The estimated effect of 100 ppb of  $\text{O}_3$  in nonasthmatic children ( $-11.9 \text{ l}/\text{min}$ ) was equivalent to 3.8% of their mean PEFR level, which was as if the absolute value of the natural increase between morning and noon did not occur. (Given that morning is the basis for comparison, the change is calculated by summing products of coefficients times variables, adding the constant, and then computing an effect/mean ratio. The natural increase in the absence of an  $\text{O}_3$  effect is the value for "noon versus morning" [ $13.1 \pm 3.6 \text{ l}/\text{min}$ ], which is similar in magnitude to the " $\text{O}_3$  \* noon" effect.)

The noon  $\text{O}_3$  effect was increased in children with asthma; estimated as the sum of effects, ( $\text{O}_3$  \* noon and  $\text{O}_3$  \* noon \* asthma) was  $-31.0 \text{ l}/\text{min}/100 \text{ ppb}$  (11.9 added to  $-19.1$ ). The large variability ( $\text{SE} = 17.9$ ) precluded statistical significance ( $p < .10$ ). Part of this variability resulted from the reduced number of noon PEFR measurements, compared with other time periods. Thus, higher  $\text{O}_3$  concentrations were related to marked suppression of the usual increase of PEFR early in the day. The  $\text{O}_3$  effect on noon PEFR values was not significant when the 8-h mean was used to estimate  $\text{O}_3$  concentrations (in Model III).

The effect of  $\text{O}_3$  on evening PEFRs was seen only in asthmatic children, and it was more pronounced when the 8-h mean was used to estimate  $\text{O}_3$  concentration instead of the 1-h maximum value (Table 1, Models III and II, respectively). This may have resulted from a delayed or cumulative response to  $\text{O}_3$  during the course of the day. The PEFR values, estimated from Model II for 1-h maximum  $\text{O}_3$ , are illustrated in Figure 2. This essentially represents the diurnal change in PEFRs for two levels of  $\text{O}_3$  in asthmatics (where 1 = asthmatics), compared with others.

Table 1.—Effects of  $\text{O}_3$  on PEFR Values ( $\text{l}/\text{min}$ ) Estimated in Random Effects Models

Factors in model	Ozone concentration (in 100 ppb) estimated as:		
	1-h maximum		8-h mean
	Model I	Model II	Model III
Time-dependent			
$\text{O}_3$ * noon	$-11.9 \pm 6.3^*$	.	.
$\text{O}_3$ * noon * asthma	$(-19.1 \pm 19.0)^{\dagger}$	.	.
$\text{O}_3$ * evening	.	$(0.2 \pm 4.7)$	$(1.2 \pm 5.4)$
$\text{O}_3$ * asthma * evening	.	$-13.8 \pm 4.9$	$-17.6 \pm 5.8$
$\text{O}_3$ * ETS * evening	.	$(-1.6 \pm 2.6)$	$(-2.0 \pm 3.1)$
Constant			
Age (y)	$25.1 \pm 1.1$	$25.2 \pm 1.1$	$25.2 \pm 1.1$
Noon (vs. morning)	$13.1 \pm 3.6$	$6.6 \pm 1.0$	$6.5 \pm 1.1$
Evening (vs. morning)	$8.0 \pm 0.8$	$8.2 \pm 2.6$	$7.8 \pm 2.6$
Asthma * morning	$(-2.90 \pm 2.4)$	$-10.9 \pm 2.8$	$-11.3 \pm 2.8$
Asthma * noon	$20.9 \pm 11.7^{\ddagger}$	.	.
Constant	$55.7 \pm 10.8$	$56.1 \pm 10.9$	$56.1 \pm 10.9$

Notes: All subjects were 15 y of age or less. All values presented as coefficient  $\pm$  standard error. Total number of subjects included = 287; total number of observations = 5 483.  
 \*Not included in the model.  
 $^{\dagger}$ ( ) effects nonsignificant but included in the model.  
 $^{\ddagger}$   $.05 < p < .10$ ; all other effects are significant ( $p < .05$ ).

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Table 2.—Effects of O<sub>3</sub> on PEFR Values (l/min) Estimated in Random Effects Models

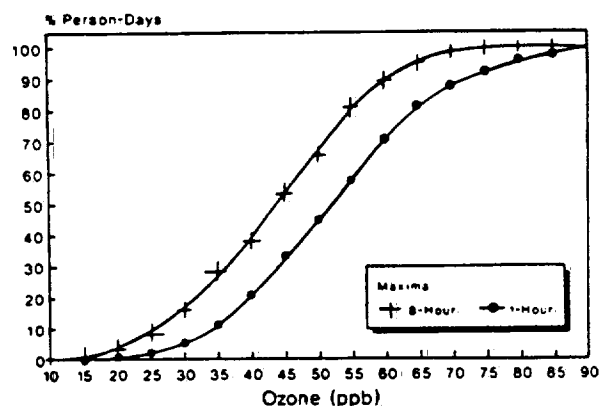
Factors in model	Ozone concentration (in 100 ppb) estimated as:		
	1-h maximum	8-h mean	
	Model I	Model II	Model III
Time-dependent			
O <sub>3</sub> * evening	(-3.7 ± 3.1)*	(-3.8 ± 3.6)	†
O <sub>3</sub> * time out * evening	†	†	(0.3 ± .05)
O <sub>3</sub> * time out * asthma * evening	-2.3 ± 1.4‡	-2.9 ± 1.6‡	-4.5 ± 1.8
O <sub>3</sub> * during 4 preceding days * asthma	†	(-19.5 ± 18.2)	†
Constant			
Females (vs. males)	-145.2 ± 4.8	-145.3 ± 6.7	-143.9 ± 6.9
Evening (vs. morning)	14.7 ± 1.9	14.4 ± 1.8	12.0 ± 0.9
Asthma * morning	-7.8 ± 2.0	-7.8 ± 1.9	-9.8 ± 2.0
Females * evening	-2.8 ± 1.0	-2.8 ± 1.0	-2.3 ± 1.1
Environmental tobacco smoke	†	†	-16.4 ± 7.2
Constant	566.3 ± 4.8	567.1 ± 4.9	571.1 ± 5.6
No. of subjects	520	520	445
No. of observations	8 122	8 118	7 224

Notes: All subjects were 15+ y. of age. All values presented as coefficient ± standard error, except as otherwise noted.  
 \*Effects nonsignificant but included in the model.  
 †Not included in the model.  
 ‡.05 < p < .10; all other effects are significant (p < .05).

In children with asthma, the estimated decrement in evening PEFRs resulting from an 8-h mean O<sub>3</sub> concentration of 80 ppb (Model III) was 4.3% of the mean evening PEFR level (calculated as before, age = 10 y). Another model (not shown, limited to 5 339 observations), which estimated O<sub>3</sub> exposure to be the product of the O<sub>3</sub> 8-h mean and the duration of time spent outdoors during that day (expressed as ppb-h), showed a significant overall effect of O<sub>3</sub> exposure in asthmatic children (-4.9 ± 1.5 l/min/100 ppb-h) and an additional O<sub>3</sub>-related decrement in evening PEFR level in children exposed to ETS at home (-2.1 ± 0.9 l/min/100 ppb-h).

In general, there was no significant relationship between morning PEFR values and ambient O<sub>3</sub> levels on the preceding day, although there was a tendency (not significant) for morning PEFR to decrease with an increasing 1-h maximum O<sub>3</sub> in asthmatic children; the variability of this effect was very large (-14.3 ± 14.8 l/min/100 ppb). No indication was found for an effect of cumulative O<sub>3</sub> exposure, estimated as an average of 8-h mean O<sub>3</sub> levels in 4 preceding days, and there was no difference between the results for asthmatic and nonasthmatic children.

In adults, no decrease in noon PEFR values was seen during the days when there were higher O<sub>3</sub> levels; the estimated effect of O<sub>3</sub>, adjusted for sex, asthma status, and diurnal variability of PEFR was +6.1 (± 3.9) l/min/100 ppb (p > .10). There was, however, an effect of O<sub>3</sub> exposure (time \* concentration) on evening PEFR—but only in asthmatics—and it was related to the amount of time spent outdoors on the days higher O<sub>3</sub> concentrations occurred (Table 2). The effects of 1-h and 8-h O<sub>3</sub> estimates were similar, and both were rather small. With regard to mean evening level, the effect of 100 ppb-h did not exceed 0.5% in men and 0.7% in wom-



Test days 2-15.

Fig. 1. Cumulative distributions of person-days by 1-h maximum and maximum 8-h mean O<sub>3</sub> concentration.

en. In 445 nonsmoking adults who had ETS exposure, the effect of O<sub>3</sub> in asthmatics—adjusted for ETS—was more pronounced (Model II in Table 2). A similar effect of O<sub>3</sub> in asthmatics (-5.1 ± 1.9 l/min/100 ppb-h) was obtained for 305 subjects in whose homes there were no smokers (5 011 observations).

In adults, there was no significant decrement in morning PEFRs that resulted from higher O<sub>3</sub> levels during 1 or during the 4 preceding days (i.e., the same as was found for children). However, the effect of mean O<sub>3</sub> level during the 4 preceding days, estimated for asthmatics (-19.5 ± 18.2 l/min/100 ppb), suggested that there might be a tendency for a more lasting response in some individuals who have asthma. These results did not change after adjustment was made for ETS.

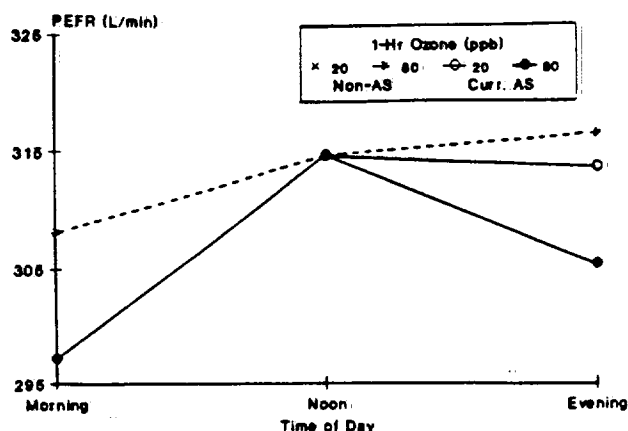


Fig. 2. Effect of 1-h maximum  $O_3$  on evening PEFR in asthmatic and nonasthmatic children, estimated by random effect models (Table 1, Model II: age = 10 y).

The PEFR values were also related independently to some of the remaining covariables considered. In children, PEFR values were reduced by  $5.6 (\pm 2.4)$  l/min on days when acute respiratory illness symptoms occurred. On hotter days, the evening PEFR levels were decreased in children (by  $1.6 \pm 0.6$  l/min/ $10^\circ F$ ), and noon PEFR levels were decreased in adults (by  $2.7 \pm 0.4$  l/min/ $10^\circ F$ ). However, these factors did not influence the relationship of PEFR with  $O_3$ . Furthermore, PEFR was not related to working near dusts or fumes or to ambient levels of  $PM_{10}$ , and there were no interactions between these factors and  $O_3$ . Results for subjects examined in March (the first month in each study year during which  $O_3$  levels exceeded 50 ppb on most days) were not different from the results for subjects examined during other seasons.

**Daily variations in PEFR and symptoms.** Daily average evening PEFR was related to maximum 8-h  $O_3$  during days in the spring, summer (without precipitation), and fall, after adjusting for significant covariables in the ANCOVA model (specifically, the proportion of children). The relationship of evening PEFR with maximum temperature was only of borderline significance ( $p = .08$ ). The interactive effect of  $O_3$  and temperature on daily average evening PEFR was also borderline ( $p = .07$ ). However, the three-way interaction of  $O_3$  \* temperature \*  $PM_{10}$  on daily average PEFR was highly significant (Fig. 3). Maximum temperature alone, and while interacting with  $PM_{10}$ , was significantly related to reduced PEFR. Increased days of observation (by removal of  $PM_{10}$  as an explanatory variable) enhanced the significance of the  $O_3$ -temperature interaction (to  $p = .005$  [Fig. 3]). Ozone alone—above 56 ppb—produced a difference of more than 12 l/min; the three-way interaction led to a reduction of more than 21 l/min, which was not quite additive. The use of season-specific, age-adjusted z-scores (standard normal deviates) yielded similar results. Effects of  $O_3$  from the previous day on average morning PEFRs were primarily in conjunction with the previous day's temperature and with  $PM_{10}$ .

There was a significant increase in symptoms associated with prolonged exposure to  $O_3$ , which was in-

dexed as the maximum 8-h average on the previous day. The effect was seen primarily for allergic-irritant symptoms (Table 3). The increase was much greater with interactions of  $O_3$  and maximum temperature and with  $PM_{10}$ . Ozone alone produced a difference of more than 7% in prevalence rates. There was also an increase in symptoms that resulted mainly from temperature; there was only a limited effect of prolonged  $O_3$  exposure. After log transformation of symptom rates, the previous day's  $O_3$  (i.e., lag one) and that day's maximum temperature were independently significant. There were no significant interactions. Other covariates and confounders (listed in the Methods section) were not significant in any of these ANCOVA models.

## Discussion

This study shows that, for children (especially asthmatics), a reduction of PEFR, measured at noon on days when high peaks of  $O_3$  concentration occur, is indicative of an immediate response of respiratory function to  $O_3$  exposure. In children and adults, and especially asthmatics, we have also found similar effects of  $O_3$  on PEFR levels measured in the evening (i.e., following several hours of elevated  $O_3$  concentration in ambient air). Often this effect was much more pronounced when elevated on a daily basis, and it was related to interactions of  $O_3$  with temperature and, sometimes,  $PM_{10}$ . Effects of  $O_3$  on daily symptom rates were also seen (specifically for allergic-irritant symptoms).

No major effect on PEFR (morning) was related to the previous day's  $O_3$  in the REM analysis; however, a trend was suggested in asthmatics (random-effects model). Changes in daily average morning PEFR values were related to the previous day's 8-h  $O_3$  in the ANCOVA analysis. Neither model revealed cumulative effects for the previous 4 d of  $O_3$  exposure. A previous time-series analysis from a different Tucson population study had not shown a lagged effect of maximum 1-h  $O_3$  on PEFR either, but had shown such lagged effects on productive cough (of 1–2 d) and wheeze (of 3 d) in asthmatics.<sup>27</sup>

It is possible that there are some longer-lasting effects of  $O_3$  on lung function,<sup>10</sup> but that their magnitude is too small to be detected in this analysis because of the variability of PEFR measurements. We performed a simulation study so that the minimum effects that were detectable with our data (REM method) could be evaluated. We assumed a linear change in PEFRs, related to  $O_3$  concentration during the preceding day, and a mean linear coefficient  $B$ . The actual value of the coefficient,  $b$ , was selected for each individual as a random number, normally distributed with mean  $B$  and standard error  $B/2$ . We calculated, for each PEFR measurement, the expected value to be a sum of the actual value and  $b \cdot (O_3 \text{ level in preceding day} - 50 \text{ ppb})$ . Several values of  $B$  were considered. The minimal simulated effect found to be significant for children by the random effects model was  $-12 \pm 6$  l/min/100 ppb. The minimal detectable effect in adults was  $-6 \pm 3$  l/min/100 ppb. The threshold values decrease when smaller variability of the effects is assumed. These results show that

Table 3.—Effect of Prior Day's Maximum 8-h PM <sub>10</sub> and Temperature on Daily Prevalence Rates (%) of Allergic/Irritant Symptoms							
Interactions/variables							
O <sub>3</sub> (ppb)	n	Adjusted* independent prev. rates (Lag one)	PM <sub>10</sub> (μg/m <sup>3</sup> )†		Max. temp. (°F)†		
			≤ 50	> 50	≤ 70	70-95	> 95
≤ 56	210	25.8%	26.9%	24.1%	25.4%	28.1%	20.1%
> 56	52	32.7%	27.2%(27)‡	37.9%(25)	(1)	33.6%(33)	26.2%(18)
Adjusted* independent		Prev. rates	27.0	27.5	27.3	29.6	21.8
p (independent) =		.011	ns			< 10 <sup>-3</sup>	
p (interaction)			.07			.03	

Note: Overall ANOVA:  $p < 10^{-3}$  ( $R^2 = 18.2\%$ ).  
 \*Adjusted for covariates (% children, smoking) and other explanatory.  
 †Max Temp — PM<sub>10</sub> interaction significant,  $p = .03$ .  
 ‡Number within parentheses denotes denominator, when  $n < 52$ .

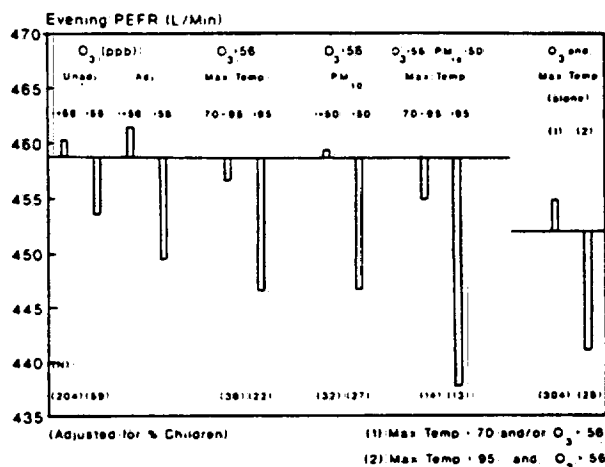


Fig. 3. Effect of 8-h O<sub>3</sub> on daily evening PEFR and interactive effects of O<sub>3</sub> with PM<sub>10</sub> and temperature, estimated by ANCOVA models.

lagged effects could have been detected if their magnitude had been similar to or greater than that of the observed short-term effects.

On many occasions, the study subjects could not measure their PEFR because limited resources allowed for only one peak flow meter per home. Thus, only 52% of subjects had data for each day, and very few of them performed all three tests each day. We wanted to assess the effect of missing data on the relationships studied; therefore, the relationship between the proportion of completed measurements, O<sub>3</sub> concentration, and subject's PEFR level was analyzed. Such analysis indicated that the noon PEFR measurement was more likely to be omitted by adults who had lower mean PEFR levels on days when there were higher O<sub>3</sub> concentrations. This could be the reason for the observed slight increase in noon PEFRs on days when there was a high 1-h O<sub>3</sub> level, and might, therefore, lead to an underestimation of the effect of O<sub>3</sub> on noon

PEFRs in adults. In children, the omission of the noon PEFR measurement was more likely to occur in those with lower PEFR levels, but that relationship was similar during days when there were various O<sub>3</sub> levels. We conclude, therefore, that the estimated effect of O<sub>3</sub> on noon PEFRs in children is not likely to be biased by the selection. Furthermore, there was no relationship between the frequency of days for which PEFR measurements were missing and the mean O<sub>3</sub> levels during the 4 preceding days, with respect to the PEFR average level. Therefore, missing data were not a factor in failing to detect prolonged-exposure effects.

The observed short-term effects of O<sub>3</sub> on noon PEFRs in children were greater than those reported previously in some chamber studies,<sup>23-25</sup> but they were smaller than the effects of O<sub>3</sub> on pulmonary function that were estimated in field studies.<sup>3-5</sup> Also, in adults, the magnitude of the decrement in PEFRs that resulted from O<sub>3</sub> was smaller than that found previously in a group of subjects who exercised.<sup>6</sup> One source of these differences may be the assessment of the O<sub>3</sub> exposure. We can assume that most subjects in this study had a lower level of activity than was observed or applied in former studies. The spatial distribution of O<sub>3</sub> concentrations in the Tucson basin was fairly uniform, but individual exposures could vary considerably because of the different patterns of daily activity. Subjects spent much of the day indoors, which possibly reduced their O<sub>3</sub> exposure; this would be especially true if they were indoors during the hours of higher O<sub>3</sub> levels. The information on time spent indoors included in the models only partially improved the estimate of exposure because this value did not identify the specific hours when the subjects were outdoors. (Subsequent studies in this population will enable examination of when the children are outdoors.) The different patterns of activity may explain, in part, the different responses to O<sub>3</sub> observed in children and in adults. Children may be more



likely than adults to be outdoors around noon and before evening, and are more likely to be exposed to elevated levels of  $O_3$  before the PEFR measurements. In adults, the effects of  $O_3$  on evening PEFRs could result from prolonged exposure, but may also result from a short-term exposure that may occur in the afternoon, shortly before their evening PEFR measurement. It appears that the afternoon  $O_3$  levels may be quite elevated during days when 8-h means are high.

In addition to this possible overestimation of  $O_3$  exposure for some subjects in our study, another factor that could have contributed to a smaller function response seen here, compared with other field studies, may be the relatively low levels of air pollutants (other than  $O_3$  and  $PM_{10}$ ) in Tucson.<sup>26</sup> These pollutants—especially acid aerosols—may have increased the response in the previous field studies.<sup>1</sup>

This analysis indicates that a more pronounced response to  $O_3$  exists in some adult asthmatics than in nonasthmatic subjects. An increased effect of  $O_3$  was seen in asthmatics in the previous Tucson study<sup>5,28</sup> and in recent laboratory experiments,<sup>29</sup> but not in other data.<sup>30,31</sup> In the present study, there was an increase in  $O_3$  effects attributed to asthma, but they were not all ways statistically significant. This was the case because of the large variability of the results in asthmatics; it is possible that an increased number of asthmatic subjects or an increased number of observations would produce more pronounced effects.

The use of medication improves morning values for asthmatics, but it has no effect on the relationship between other air pollutants and PEFR.<sup>32</sup> In the current study, the only significant correlation between medication use and level of  $O_3$  was seen in male asthmatics who were 35 y and older: 48% used breathing medication on the days when there was 1-h  $O_3$  levels of 65 ppb or more, compared with 19% on other days ( $p < .01$ ). The corresponding percentages of subjects who used medications on days when there were 8-h  $O_3$  levels of 65 ppb or more, versus days when there was less than 65 ppb, were 41% and 26%, respectively ( $p < .01$ ). The use of medications on days when there were higher  $O_3$  levels may have minimized our result in adults, especially in asthmatics. Use of medication increased PEFRs on days when there was low  $O_3$ , but it did not increase PEFRs on days when there was high  $O_3$ . An ANCOVA demonstrated that the effect of maximum 8-h  $O_3$  on the reduction of PEFR was still significant ( $p < .05$ ), but that the effect of the medication and the interaction of medication use with  $O_3$  were not significant ( $p > .10$ ).

The lack of a consistent cumulative effect of elevated  $O_3$  for a few days could be expected if a functional adaptation of the respiratory system occurs, as was found previously for an  $O_3$  concentration that exceeded 350 ppb.<sup>33-35</sup> However, such adaptation, if it exists, did not modify the short-term responses to  $O_3$  in our study. Also, the analysis of seasonal effects does not support the hypothesis of a longer-lasting adaptation. Our choice of March as the possible time for a greater "spring" response was based on analysis of  $O_3$  levels. Between November and February, the number of days

during which maximum 1-h  $O_3$  levels exceeded 50 ppb were only 3–10/mo, whereas in the remaining months this number exceeded 23. The lack of an effect of season in the REM analysis might have resulted from the crude identification of the time when an increased response to higher  $O_3$  occurred, or perhaps from a too short time period in which there were low levels of ambient  $O_3$ . When daily values (in the ANCOVA) were restricted to the  $O_3$  season in Tucson (i.e., spring, dry summer, fall), the effects were more evident than if using the entire year. Therefore, it is unlikely that negative findings would result from a small, but significant, adaptation process in the Tucson population.

The analyses also controlled for SES, crowding, cigarette smoke (ETS) exposure, gas stoves, and actual monitoring results. Our results, therefore, were not spurious, based on the exposure assessment used, nor were they based on uncontrolled effect-modifiers or confounders.

In conclusion, our results indicate that short-term effects of ambient  $O_3$  at concentrations below the current standard (120 ppb) can be observed during the normal activity of a community population.

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## asbestos victims special fund trust

### REQUEST FOR GRANT APPLICATIONS

The ASBESTOS VICTIMS SPECIAL FUND TRUST, a charitable organization concerned with the medical, legal, and social implications of exposure to asbestos, is accepting applications for research efforts relevant to the health effects of asbestos exposure. Applications must be submitted on or before May 1, 1992. To obtain further information and application materials, please contact the Asbestos Victims Special Fund Trust, 1500 Walnut Street, Suite M-11, Philadelphia, PA 19102, (800) 447-7590.

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Gelber, L.E., Seltzer, L.H., Bouzoukis, J.K., Pollart, S.M., Chapman, M.D., and Platts-Mills, T.A.E., "Sensitization and Exposure to Indoor Allergens as Risk Factors for Asthma Among Patients Presenting to Hospital," American Review of Respiratory Disease 147(3): 573-578, 1993.

The authors of this study investigated the potential role of indoor allergens in adult patients with acute asthma. A case-control study of 114 patients and 114 controls presenting to an emergency room (for asthma and conditions other than breathlessness, respectively) was conducted. The authors reported that "thirty-eight percent of the asthmatics, but only 8% of the control subjects, were allergic to one of the three indoor allergens, and had high levels of the relevant allergen in their houses (odds ratio, 7.4; confidence interval, 3.3 to 16.5)." The authors concluded that "the results suggest that the risk for asthma related to sensitization to indoor allergens applies to a large proportion of adults with acute asthma" and that "this risk is prominent among the socioeconomic groups that have suffered the largest increase in both morbidity and mortality from asthma."

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## Sensitization and Exposure to Indoor Allergens as Risk Factors for Asthma among Patients Presenting to Hospital

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To investigate the role of indoor allergens in adult patients with acute asthma, we conducted a case-controlled study on patients presenting to an emergency room. One hundred and fourteen patients and 114 control subjects were enrolled over a 1-yr period in Wilmington, Delaware. Sera were assayed for total IgE, and for IgE antibodies to dust mites, cat dander, cockroach, grass pollen, and ragweed pollen. Dust was obtained from 186 homes and assayed for dust mite, cat, and cockroach allergens. IgE antibodies to mite, cat, and cockroach were each significantly associated with asthma, and this association was very strong among participants without medical insurance and among African Americans. Among 99 uninsured participants, sensitization to one of the indoor allergens ( $> 200$  RAST units) was present in 28 of 57 asthmatics and in one of 42 control subjects (odds ratio, 39; confidence interval, 9.4 to 166). For cat and cockroach the combination of sensitization and presence of allergen in the house was significantly associated with asthma. Furthermore, there was a strong inverse relationship between IgE antibodies to cat and to cockroach, and the risk of this sensitization was in large part restricted to homes or areas with high levels of allergen. Thirty-eight percent of the asthmatics, but only 8% of the control subjects, were allergic to one of the three indoor allergens, and had high levels of the relevant allergen in their houses (odds ratio, 7.4; confidence interval, 3.3 to 16.5). The results suggest that the risk for asthma related to sensitization to indoor allergens applies to a large proportion of adults with acute asthma and that this risk is prominent among the socioeconomic groups that have suffered the largest increase in both morbidity and mortality from asthma.

An increase in the severity of asthma during the past 20 years has been observed in several countries, but it has been particularly marked in urban areas and among African American populations in the United States (1-3). Over the same period it has been shown that asthma is an inflammatory disease of the bronchi characterized by eosinophil infiltration (4-6). In keeping with this model of asthma, experimental exposure of the lungs of sensitive patients to allergens can release inflammatory mediators, recruit eosinophils, and increase bronchial reactivity (7-9). This has led to the argument that year-round exposure to allergens may be important as a cause of bronchial hyperreactivity. Thus, it appears that the relationship between allergen exposure and asthma can be divided into two phases: exposure of genetically predisposed persons most commonly in childhood that leads to sensitization, and ongoing exposure of sensitized persons that contributes to chronic bronchial hyperreactivity (10-12). Given that most people spend 20 to 22 hr per day indoors and at least half this time in their own homes, it is not surprising that increasing attention has focused on the role of foreign proteins that accumu-

late in houses (13-17). During the last 10 years population and clinical studies from many different parts of the world have established that exposure to allergens derived from the dust mite *Dermatophagoides pteronyssinus* is associated with sensitization and asthma (18-21).

Most previous epidemiologic studies have not included a sufficient number of asthmatics with acute disease to answer whether sensitization to indoor allergens was relevant to these patients. For this reason it is often implied that allergen exposure is relevant only to mild or seasonal asthma. Our previous study in Charlottesville, Virginia showed that sensitization to indoor allergens was associated with asthma (16). However, that study did not include any results on allergen exposure. Indeed, there has been no quantitative data relating exposure to indoor allergens other than dust mite to asthma. Furthermore, there has been very little data on the levels of allergen in houses of lower income patients. Recently, monoclonal antibodies to cat and cockroach allergens have been developed so that it is now possible to measure allergens derived from three separate sources in house dust (22-25). The present case control study investigated serum IgE antibodies and the levels of allergen in the houses of random adult asthmatics presenting to hospital emergency rooms in Wilmington, Delaware. The catchment area for these patients included both inner city and suburban zones.

### METHODS

One hundred and fourteen patients 15 to 55 yr of age who presented to either of two emergency rooms in Wilmington with asthma were enrolled

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Am Rev Respir Dis Vol 147: pp 573-578, 1993

between September 1988 and June 1989. An equal number of age- and sex-matched control subjects were enrolled who presented to the same two emergency rooms (ER) within 1 wk of the patients with any condition other than breathlessness. Demographic data on the patients and control subjects (including details of medical insurance and smoking history) were taken from the hospital charts and from a questionnaire completed in the ER and confirmed at house visits. Asthmatics were patients presenting to the ER with breathlessness for whom the physician on call prescribed urgent treatment for airway obstruction. Airway obstruction was confirmed in all cases by measurement of peak expiratory flow rate, and in 110 cases reversal of obstruction was confirmed by  $\geq 20\%$  increase after therapy. Peak expiratory flow rates were measured before and after treatment: for the 114 asthmatics values were  $193 \pm 99$  and  $320 \pm 126$  L/min (arithmetic mean  $\pm$  SD), respectively.

Serum was obtained from each subject and was assayed for total IgE and for specific IgE antibodies. Total serum IgE levels were measured by two-site monoclonal-antibody-based assay; the geometric mean value for the patients with asthma was 160 IU/ml, and for the control subjects it was 44 IU/ml (paired  $t$  test;  $p < 0.001$ ). Among the asthmatics, only 21 had total serum IgE  $< 40$  IU/ml, whereas 59 control subjects had levels below this. In keeping with previous studies, the increased levels of IgE were present in all age groups (16, 26). IgE antibodies were measured by a quantitative RAST technique using allergen extracts coated to cyanogen bromide activated cellulose discs as described previously (16). The allergens used were dust mites (*D. pteronyssinus* and *D. farinae*), cat (*Felis domesticus*) epithelium, cockroach extract (German, American and Oriental mixed), short ragweed pollen, and rye grass pollen. Extracts were obtained from Hollister-Stier (Spokane, WA). For each allergen the extract applied to the discs was standardized by measurement of major allergen content of the extract (16). Values for IgE antibodies were obtained from a standard curve using serial dilutions of a serum containing 1,000 units of IgE antibodies to *D. farinae*. Horse serum (50%) was used as a diluent to reduce nonspecific background. Preliminary studies confirmed that horse serum did not inhibit binding to any of the allergens studied. The units are standardized relative to an antimitic serum pool (NIBSC 82/528), which contains 1,800 RAST units of IgE antibodies to *D. farinae*; 1 RAST unit equals approximately 0.1 ng of IgE antibody (16, 27). In addition, the sera were assayed for IgE antibodies to the fungi *Alternaria* and *Aspergillus*, using commercial (Hollister-Stier) extracts; the results for these fungi were scored on a semiquantitative basis, and 2+ results were regarded as positive.

The houses of 93 patients and 93 control subjects were visited within 2 wk of enrollment in the study. By examining the housing conditions, it was possible to differentiate urban, i.e., predominantly overcrowded or rundown housing, from suburban housing. The urban boundary of Wilmington (an area of approximately 35 square miles) was defined by a long-time resident of New Castle County with extensive knowledge of local demographics. The area included the whole of postal areas 19701, 19720, 19801, 19802, 19805, and 19806, and it also included sections of 19804 and 19808 extending approximately half a mile on either side of route 2. Four dust samples were collected from each home using a handheld Douglas<sup>®</sup> vacuum cleaner modified with a cotton filter. The samples were obtained from bedding, bedroom carpets, sofas, and kitchens. The kitchen samples were obtained by vacuuming the accessible cabinet space above, below and adjacent to the kitchen sink and the surface of the floor adjacent to the kitchen cabinets. The remaining samples were collected by vacuuming a 1 square meter area for 2 min. Families were questioned about, and houses were examined for, the presence of cockroaches. Dust samples were assayed for Group I dust mite allergens (*Der f* I and *Der p* I), cat allergen (*Fel d* I), and for a German cockroach allergen, *Blattella germanica* allergen II (*Bla g* II), using two-site, monoclonal-antibody-based ELISA (23–25). The details of the assays have been reported elsewhere; the detection limits for the assays were 0.2  $\mu$ g/g for *Der p* I and *Der f* I, 0.2  $\mu$ g/g for *Fel d* I, and 0.5 units/g for *Bla g* II. In analyzing the results the highest level for each allergen (out of four samples) in a house was taken as an index of exposure to that allergen (10). Cutoff values for considering levels as significant were chosen based on previous results and the present study; for cat allergen  $\geq 8$   $\mu$ g *Fel d* I/g dust; for cockroach allergen  $\geq 2$  units *Bla g* II/g dust; for dust mite allergen  $\geq 10$   $\mu$ g Group I mite allergen/g of dust (10).

Odds ratio was calculated as the odds of disease occurring in persons with IgE antibodies, relative to the odds of disease occurring in those without IgE antibodies. Analysis of the data for sensitization and allergen exposure was for unmatched data since not all the houses were visited. Values for etiologic fraction (defined as the proportion of all cases in the target population attributable to a given risk factor) were obtained using the equation proposed by Schlesselman (28).

## RESULTS

### Sensitization and Relationship to Other Demographic Factors

Measurement of serum IgE antibodies by RAST demonstrated that for each of the five common inhalant allergens the prevalence of sensitization was greater among asthmatics than among control subjects (figure 1). As expected for atopic persons, some patients (and control subjects) had IgE antibodies to multiple allergens. Sensitivity (defined as IgE antibody  $> 40$  RAST units) to at least one of the five inhalants was present in 83 of 114 asthmatics and 42 of 114 control subjects. For the three indoor allergens results for IgE antibodies were analyzed at levels of 40 and 200 RAST units, and the results for uninsured participants and for African Americans were analyzed separately (table 1). The results show that in these groups there was a very strong association between sensitivity to indoor allergens and asthma. In particular, for the uninsured, there were 28 asthmatics with  $> 200$  units of IgE antibody and only one control subject with a comparable level (odds ratio, 39; confidence interval, 9.4 to 166). In addition to race and insurance status, information was available about the geographic location of housing. Geographic location, race, and insurance status were each strongly related to each other, and this applied equally to asthmatics and control subjects (table 2). For example, in the urban area among the uninsured, 48 were nonwhite and 13 were white. By contrast, in the suburban area among the insured, 78 were white and 11 were nonwhite. Smoking histories showed no relationship to disease. Among 49 patients who presented with asthma and who had no detectable IgE antibodies to one of the three indoor allergens, 23 were active smokers and seven were passive smokers (overall, 61%). The figures for smoking were very similar among all asthmatics (66 of 114 or 58%) and also among the whole population (139 of 228 or 61%).

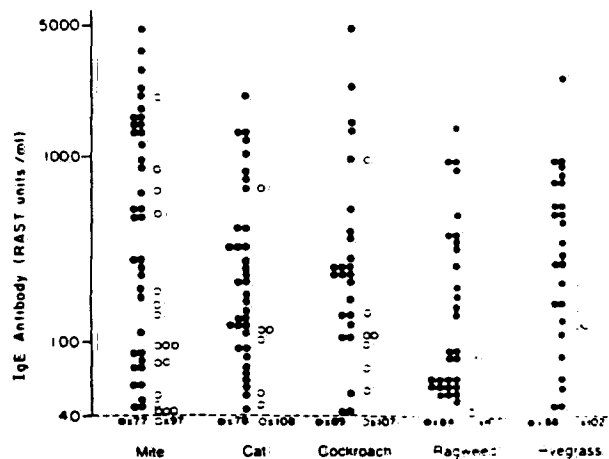


Figure 1. IgE antibodies to five common allergens in sera from 114 patients presenting with asthma (closed circles) and 114 age- and sex-matched control subjects (open circles). The numbers given below the level of 40 units/ml are the numbers of patients and control subjects with less than this level. The RAST units of IgE antibody are approximately equivalent to 0.1 ng IgE.

TABLE 1  
SENSITIZATION TO ONE OF THE INDOOR ALLERGENS AMONG ASTHMATICS AND CONTROL SUBJECTS\*

	RAST (units)	All Patients		Uninsured		African American	
		Asthmatics (n = 114)	Control Subjects (n = 114)	Asthmatics (n = 57)	Control Subjects (n = 42)	Asthmatics (n = 46)	Control Subjects (n = 42)
Sensitization to one of three indoor allergens	> 40	65	23	34	8	32	10
	> 200	44†	5	28	1	26	1

\* Sensitization was judged by serum IgE antibodies and evaluated at levels of > 40 and > 200 RAST units/ml.

† Among patients with > 200 RAST units specific for at least one of the three indoor allergens, the results for asthmatics and control subjects were: mite, 24/4; cat, 18/1; cockroach, 16/1.

#### Concentrations of Dust Mite, Cat, and Cockroach Allergens in House Dust

Dust samples were obtained from 186 houses (four samples per house): 93 asthmatics and 93 control subjects. Of the 186 houses studied 98 had greater than the proposed threshold levels of cat or cockroach allergen. Fifty-seven houses were found to have significant cat allergen ( $\geq 8 \mu\text{g Fe} d \text{ I/g dust}$ ) (table 3); 75% of these houses were in the suburban area, and only 25% were in urban locations. In contrast, of 68 houses with cockroach allergen ( $> 2$  units *Bla g II/g dust*), 84% were urban, and only 16% were suburban. This difference was highly significant statistically (chi-square,  $p < 0.001$ ). Only 46 of the houses contained greater than  $10 \mu\text{g}$  Group I mite allergen/g, and there was no significant difference between urban and suburban houses ( $p = 0.31$ ). In keeping with previous results, the highest levels of mite allergen were most commonly found in bedding (32%) or in living rooms (48%); in only 3% of houses was the highest level of mite allergen found in the kitchen. By contrast, the highest levels of cockroach allergen were generally found in the kitchen samples (i.e., in 53 of 68 houses or 78%) (figure 2). In analyzing the results, the levels of

allergen in dust were taken as an index of exposure; 66% of control subjects and 74% of asthmatics had significant exposure to one of the three indoor allergens. These results suggest that current exposure alone was not a major risk factor for asthma.

#### Exposure and Sensitization

Among the 15 participants with both exposure to cat allergen and sensitization ( $> 40$  RAST units/ml), all but one presented with asthma (estimated odds ratio, 16.3; confidence interval, 3.4 to 78). Similarly, among the 19 with both sensitization ( $> 40$  RAST units/ml) and exposure to cockroach, 16 presented with asthma (estimated odds ratio, 6.2; confidence interval, 1.9 to 19.5). Comparable figures for mite sensitization and exposure were 11 asthmatics and three control subjects. A striking feature of the results was the inverse relationship between cat and cockroach allergen levels (table 4) and the complete lack of relationship between IgE antibody to cat and cockroach allergens (table 5). By contrast, among patients

TABLE 2  
DEMOGRAPHICS OF PATIENTS ENROLLED IN THE STUDY

Race*	Insurance†	Location	
		Urban	Suburban
White	No	13	29
	Yes	20	78
Nonwhite	No	48	9
	Yes	20	11

\* The nonwhite patients included six Hispanics.

† Insurance status was derived from hospital records; 11 patients with Medicaid were included with uninsured patients, but one patient with Medicare was included as insured.

TABLE 3  
LEVELS OF CAT ALLERGEN IN HOUSES WITH OR WITHOUT CATS PRESENT\*

Cat Allergen <i>Fel d I</i> † ( $\mu\text{g/g dust}$ )	Cat Present	No Cats in the House
> 80	37 (19/18)	0
> 8-80	12 (8/4)	8 (3/5)
> 1-8	0	54 (26/28)
$\leq 1$	0	75 (37/38)

\* Values in parentheses indicate the number of patients and control subjects, respectively in each category.

† Values for cat allergen were the highest level found in any sample from the house.

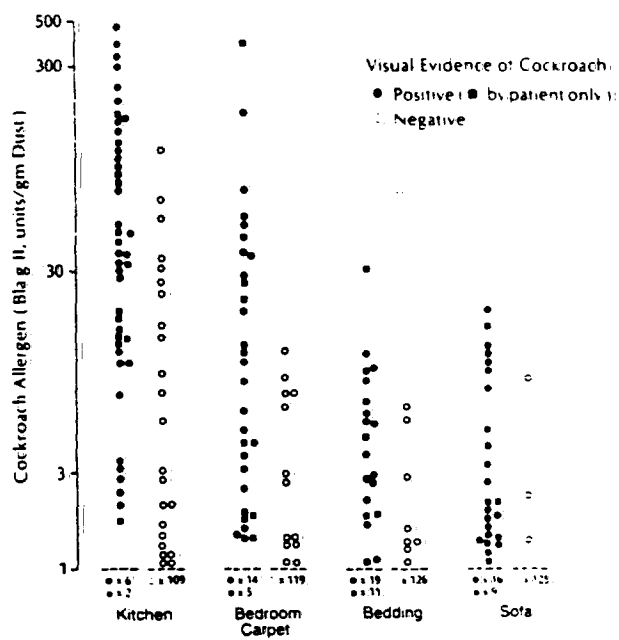


Figure 2. Levels of cockroach allergen *Bla g II* (units/g dust) in dust obtained from 186 houses. In general, houses with visual evidence of cockroach infestation (closed circles) or reported infestation (closed squares) had raised levels of allergen. However, cockroach allergen at high levels was found in some houses with no signs of infestation or report of infestation (open circles).

TABLE 4

COCKROACH (*Bla g II*) AND CAT (*Fel d I*) ALLERGEN LEVELS IN DUST FROM THE HOUSES OF PATIENTS AND CONTROL SUBJECTS\*

Highest Level of Cockroach Allergen <i>Bla g II</i> (units/g)	Highest Level of Cat Allergen <i>Fel d I</i>		
	< 8 (μg/g)	≥ 8 (μg/g)	≥ 80 (μg/g)
≥ 20	33 (18:15)	2 (1:1)	2 (2:0)
≥ 2 < 20	23 (16:7)	5 (3:2)	3 (0:3)
< 2	115 (50:65)	13 (7:6)	32 (17:15)

\* Values for each allergen are in each case the highest level found in any sample from the house. The probability of finding > 2 units of cockroach allergen was inversely related to the concentration of cat allergen,  $p < 0.001$ , using chi-square test for trend. Values in parentheses indicate the number of patients and control subjects in each group.

TABLE 5

SENSITIZATION (SERUM IgE ANTIBODY) TO COCKROACH AND CAT ALLERGEN AMONG PATIENTS AND CONTROL SUBJECTS\*

IgE Antibody to Cockroach Allergen (RAST units/ml)	IgE Antibody to Cat Allergen†		
	< 40 (RAST units/ml)	≥ 40 < 200 (RAST units/ml)	≥ 200 (RAST units/ml)
≥ 200	14 (13:1)	2 (2:0)	1 (1:0)
≥ 40 < 200	12 (6:6)	2 (2:0)	1 (1:0)
< 40	160 (59:101)	19 (14:5)	17 (16:1)

\* Serum IgE antibodies measured by RAST. The units are approximately equal to 0.1 ng IgE antibody. Values in parentheses indicate the number of patients and control subjects, respectively, in each category.

† The probability of finding sensitization to cockroach allergens (> 40 units) was unrelated ( $p = 0.8$ ) to the presence of sensitization to cat. By contrast, among patients with sensitization to mite allergen, there was a significant increase in sensitization to either cat ( $p < 0.01$ ) or cockroach allergen ( $p < 0.001$ ).

with sensitization (i.e., > 40 RAST units/ml) to mite allergens, there was a significant increase in sensitization to cat ( $p < 0.01$ ) or to cockroach allergen ( $p < 0.001$ , chi-square). Comparing urban and suburban areas, it was clear that the combination of cat exposure and sensitization was associated with asthma in the urban area (table 6). As discussed previously, race, insurance status, and geographic location were each interrelated, and this applied also to asthmatics. The combination of sensitization and relevant ex-

posure to at least one of the indoor allergens was found in 35 of 93 asthmatics and seven of 93 control subjects. When this combination was analyzed for uninsured patients the figures were 22 of 48 asthmatics and two of 20 control subjects (odds ratio, 7.6; confidence interval, 1.8 to 31).

## DISCUSSION

There are many factors that can contribute to bronchial hyper-reactivity or trigger acute attacks of asthma among patients with underlying BHR. The present study was designed to investigate the role that indoor allergens play in asthmatics presenting to hospitals, particularly among uninsured and/or urban populations. Wilmington was chosen because it is one of the larger towns in the United States where it is easy to visit houses in the urban area. Other risk factors were not addressed, e.g., air pollution, dietary factors, and the role of acute viral infections. Our study was not designed to study the effect of outdoor air pollution since the patients and control subjects were enrolled within a few days of each other. However, analyzing the admission figures for the Wilmington hospitals did not indicate peaks that could be related to changes in air pollution. Smoking histories showed no relationship to asthma in our study population. This is in keeping with the results of a recent population study in the United States (26).

The allergens studied here were chosen both from the results of skin testing in clinics in Delaware and Virginia and because it is possible to measure dust mite, cat, and cockroach allergen in house dust. There are many other allergens that also may play a role in individual cases. We found a significant number of patients with sensitivity to *Alternaria* (15 patients and five control subjects), and this may be an underestimate because enrollment was predominantly in the fall and spring, i.e., not the peak period for *Alternaria* spores (29). We consider, based on the results of skin testing, that other outdoor allergens are unlikely to account for more than 10% of cases in this area.

In analyzing the relationship between asthma, sensitization, and exposure, it was necessary to define thresholds both for IgE antibodies and allergen levels. The reason for a cutoff of 40 RAST units for IgE antibody was primarily to exclude effects of total IgE on RAST background (16). Using a higher cutoff, i.e., 200 RAST units, increased the specificity but reduced the sensitivity of the association between indoor allergens and asthma. The level of mite allergen in house dust that increases the risk of symptomatic asthma (> 10 μg Group I allergen/g) was proposed by an international workshop, and it has been reaffirmed by several re-

TABLE 6  
GEOGRAPHIC SEPARATION OF THE RISK FOR ASTHMA ASSOCIATED WITH CAT AND COCKROACH EXPOSURE AND SENSITIVITY

	Cockroach			Cat		
	Exposure*	IgE ab†	IgE ab & Exposure‡	Exposure*	IgE ab†	IgE ab & Exposure‡
Urban area						
Asthmatics, n = 43	32	16	15	8	12	4
Control subjects, n = 38	21	4	3	6	0	0
Suburban area						
Asthmatics, n = 50	8	5	1	22	16	10
Control subjects, n = 55	7	1	0	21	5	1

\* Exposure to cockroach was considered to be present in houses where at least one dust sample had > 2 units *Bla g II*/g dust. Exposure to cat allergen was considered to be present where at least one sample had > 8 μg *Fel d I*/g dust.

† IgE antibody (IgE ab) levels > 40 units/ml were considered to represent significant sensitization.

‡ The association between sensitization and exposure to cockroach allergen and asthma was significant in the urban area ( $p < 0.05$ ) but not in the suburban area. The association between sensitization and exposure to cat allergen was significant in the suburban area ( $p < 0.05$ ) but not in the urban area. The difference between the results for the two allergens was highly significant ( $p < 0.001$ ).



cent studies (10, 12, 20, 30). The levels of mite allergen found in the houses were lower than we had expected, probably because the summer of 1988 was very dry. The value used for cat allergen 8  $\mu\text{g/g}$  is a level at which almost all patients allergic to cats experience symptoms and it is the minimal level found in a house with a cat. This value has been reported in several studies, and it could be taken as a proposed threshold. The level for cockroach allergen was based on sampling approximately 350 houses in Charlottesville, Virginia; Atlanta, Georgia; and the present study, as the level that best distinguishes significant cockroach infestation. The relevance of these proposed thresholds for cat and cockroach exposure is supported by the inverse relationships seen in tables 4 and 5. Thus, patients who are exposed to cat allergen generally have < 2 units *Bla g* II cockroach allergen in their house dust, and they do not become sensitized to cockroach allergens. Furthermore, none of 65 children in England who were followed for 10 yr developed IgE antibodies to cockroach allergens, and none of the dust samples contained > 2 units *Bla g* I (12, 25). Similarly, patients who live in the inner city have less than threshold levels of cat allergen, and they generally do not develop sensitivity to cat allergen. The clinical significance of threshold levels is increased because it is possible to change the levels of allergen in houses. Mite allergen levels can be controlled either by house design (e.g., no carpets, low humidity, good ventilation) or by a combination of physical measures and the use of acaricides (22, 31). For cat allergen it appears that the factors influencing airborne allergen, and methods of reducing exposure, are completely different from those for dust mites. Recent evidence suggests that it is possible to reduce cat allergen levels even with the cat present (32, 33). It is important to evaluate whether the available methods for killing cockroaches can reduce allergen levels below 2 units/g.

Although it is not possible to prove that the relationship between sensitization to indoor allergens and asthma is causal, the evidence increasingly suggests that exposure to indoor allergens is a major cause of asthma. First, the association between asthma and sensitization has been consistently reported from many parts of the world, and it is extended by our data from Wilmington and Charlottesville to patients presenting with acute asthma. Second, the association is very strong (see table 1). Third, it is well established that inhaling dust mite, cat, or cockroach allergens experimentally can provoke both bronchospasm and inflammatory changes in the lung. Finally, intervention studies have demonstrated improvement in asthma when patients have been moved to an environment with low allergen levels, or their houses have been changed (10, 22, 34). The present results do not establish a role of current exposure to indoor allergens since the levels of cat and cockroach allergens were probably stable and the mite allergen levels did not show their normal seasonal rise in the fall of 1988. However, the results do demonstrate for the first time that many of the patients presenting to the ER were both sensitized to and had exposure to a relevant allergen in their homes. Thus, although sensitization is strongly associated with asthma, and there is a quantitative relationship between exposure and sensitization, the present data do not establish, or refute, a quantitative relationship between current exposure and the risk of acute asthma among sensitized persons. Indeed, our results could equally be explained if chronic exposure to indoor allergens maintained bronchial hyperreactivity and acute attacks were precipitated either by a large dose of allergen or a variety of other "trigger factors," including viral infection, tobacco smoke, emotional factors, etc.

Using the Wilmington and previous Charlottesville data, and assuming that the control population in the ER reflects the population from which the asthmatics came, we used the equation for

etiologic fraction proposed by Schlesselman (28). For these calculations the results of two ER studies were combined so that values are based on 188 asthmatics and 202 control subjects. 16). Sensitization to one of the five allergens gave an etiologic fraction of 46%, whereas sensitization to one of the indoor allergens gave a value of 40%. The population of New Castle County between the ages of 15 and 55 yr is estimated to be 256,000, which is ~ 0.18% of the population this age in the United States (35). During the year ending May 1989, 663 patients were treated for acute asthma in the Medical Center of Delaware, which we estimate was two-thirds of the cases treated in the County. These figures suggest that there may be as many as 550,000 ER visits/year in the United States among people 15 to 55 yr of age. From the calculated etiologic fraction, i.e., 40%, this suggests that among this age group as many as 200,000 episodes of acute asthma/year might be attributable to that risk which is associated with sensitization to mite, cat, or cockroach allergens. Our results suggest that among African American or uninsured adult patients the risk associated with indoor allergens is at least as strong as in the whole population. Furthermore, similar data for children with asthma in an inner city have recently been reported (36). Given the evidence that the prevalence and mortality of asthma in inner cities is both higher and increasing, it is clearly important to identify potentially treatable causes of asthma in this population. Our results suggest that housing conditions play an important role in asthma among lower income populations, and they also imply that recognition of this risk and education about methods of reducing it should be part of the management of the disease.

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## Environmental Tobacco Smoke: Causative Agent or White Elephant?

THE POSSIBLE EFFECTS of environmental tobacco smoke (ETS) continue to be of concern to researchers, public health administrators, and the general public. In this issue, Roy J. Shepard presents a review of respiratory irritation and ETS. He concludes, primarily on the basis of experimental challenge studies, that ETS causes only small, immediate changes in respiratory function. However, he finds that evidence, derived mainly from epidemiological studies, suggests that these acute changes may progress to chronic reactions and an increased prevalence of chronic respiratory disease. The review is a logical interpretation of the literature, and the conclusions accord with those of previous reviews,<sup>1</sup> the official policy, and public opinion.

Can we see, in spite of this, any clouds on the horizon? When most scientific data are considered, and perhaps particularly data from epidemiological studies, expert opinion may be divided. From a scientific point of view, it is extremely important that such diverse opinions—in this case, on ETS and respiratory disease—continue to be discussed, regardless of whether they support the Environmental Protection Agency, the tobacco industry, or the politician. Only by presenting sound scientific data and continuously scrutinizing its validity can proper public health measures be recommended, evaluated, and revised.

As a toxicologist, I have always been concerned by the rather extensive damage to the lungs attributed in some studies to ETS exposure. In the 1960s, it was demonstrated in animal experiments, by Green et al.<sup>2</sup> and ourselves,<sup>3</sup> that the lung's defense mechanisms are capable of sustaining relatively high doses of inhaled agents—including live bacteria—before damage occurs. Subsequent experiments on tobacco smoke<sup>4</sup> demonstrated that, at low levels of exposure, there may even be a stimulating effect on the immune function. In this perspective, extensive pulmonary effects from the rather low levels of ETS exposure found in some studies can be questioned.

I am also concerned as an epidemiologist. In the literature, a wide range of disparate health conse-

quences, including breast cancer and other diseases unrelated to active smoking, have been associated statistically with ETS exposure.<sup>1</sup> The biological plausibility that ETS causes such a wide variety of effects, and particularly effects not found to be associated with active smoking, must be rather low. Also, for certain diseases, e.g., cardiovascular disease, the increased risk related to ETS is of about the same order as that related to active smoking.

Could it be that we are committing a fundamental error by placing ETS in the category of a causative factor, when in reality we may be studying a confounder? There are two aspects to this issue. First, the general problem of confounding becomes particularly important in studies of weak associations, or low-risk agents such as ETS. This was reviewed extensively by Wynder<sup>5</sup> several years ago. With regard to respiratory infections and ETS exposure, the classic study from Jerusalem<sup>6</sup> demonstrated that social factors were three to four times more important than ETS exposure, although the latter was significantly related to the disease. In all studies on weak associations, the major causative factor must be very precisely described before any certain conclusions concerning less important factors can be drawn—a task that has not been carried out successfully in several of the studies reviewed.

The second aspect relates to new confounders that were unknown at the time of the different studies. There is increasing evidence that dietary habits are related to several kinds of respiratory disease, including lung cancer and chronic bronchitis.<sup>7,8</sup> Evidence also exists that smokers' diets differ from nonsmokers', and there are studies that suggest these differences are present in nonsmoking females, whether married to smokers or nonsmokers.<sup>9</sup> Consumption of fat or smoked foods increases the risk; vegetable and fruit consumption decreases it.

It is too early to conclude how these possible confounders, or any other potential confounders, could influence the conclusions drawn in Shepard's review. It will be interesting, however, to see how well they stand

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up to critical assessment in 5 or 10 y, when results are available from ongoing studies that include dietary habits.

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# **FURTHER ANALYSES OF THE ROLE OF CONFOUNDING VARIABLES IN EPIDEMIOLOGIC STUDIES OF ENVIRONMENTAL TOBACCO SMOKE AND THE RESPIRATORY SYSTEM IN SCHOOL-AGE CHILDREN.**

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**Key Words:** Respiratory disease in children, Pulmonary function, Environmental tobacco smoke (ETS), Parental Smoking, Respiratory infection, Asthma, Epidemiology, Confounding variables

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## **ABSTRACT**

A series of analyses that we have conducted to date reveal little to no consistency from study to study in the association between parental/household smoking and specific respiratory endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) or pulmonary function parameters (such as FEV<sub>1</sub>, FEF<sub>25-75</sub>, and Vmax<sub>50</sub>) in school age or older children. We have suggested that these inconsistencies could reflect variability in the potential confounders that were considered in the studies in question. Accordingly, we have been examining the extent to which 21 predetermined potential confounding variables were addressed in the 45 clinical endpoint and 38 pulmonary function endpoint studies in question. A previous report

examined 5 of the variables, the current report pertains to the remaining 16. This analysis reveals that there is a wide variation in the criteria used for several of the confounders under examination, most notably family size, location of residence, age of the subject, active smoking, outdoor pollution, dampness and cold, type of heating/air conditioning, and quality of housing. Selected confounders were found to be consistently associated with increased prevalence of respiratory symptoms and disease (male gender), increased pulmonary function (age, male gender, or decreased pulmonary function (active smoking, location of residence)). With regard to associations between clinical and pulmonary function endpoints and the remaining confounders examined here, associations were either not observed, of an uncertain nature, or could not be determined. The lack of standardization in the treatment of confounding variables, as well as the apparent influence of certain of these factors, could be responsible for the inconsistency from study to study of the association between parental/household smoking and respiratory clinical and pulmonary function endpoints in school-age and older children.

## INTRODUCTION

We recently reported an updated and expanded analytical review of the literature pertaining to the relationship between parental/household smoking (as a surrogate for ETS exposure) and the respiratory system of school-age or older children, which involved 45 clinical endpoint studies and 38 pulmonary function endpoint studies [1]. As in our earlier analyses that had been done on a smaller, more limited database [2,3], this recent analysis indicated little to no consistency from study to study in the association between this surrogate for ETS exposure and specific respiratory endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) and such pulmonary function parameters as FEV<sub>1</sub>, FEF<sub>25-75</sub>, and Vmax<sub>50</sub> [1].

Since potential confounding variables (i.e., other factors that might co-vary with the independent variable) are recognized as important factors that can affect the outcome of an epidemiologic study [4-6], we have suggested that this lack of consistency could reflect the variability with which potential confounders were considered in the studies in question [1-3]. We have also suggested that the lack of verification by physician examination or medical records of parental responses to questionnaires regarding specific respiratory symptoms and diseases could contribute to inconsistencies observed from study to study with regard to clinical endpoints [1-3].

As a result of these considerations, we recently initiated further analyses to determine the extent to which 21 pre-determined confounding variables were addressed in the 45 clinical endpoint and 38 pulmonary function endpoint studies in question, as well as determining the frequency with which clinical endpoints were verified (i.e., by medical examination or medical records) in the former. An initial report of this further analysis dealt with the frequency with which these clinical endpoints were verified, the frequency and consistency with

which these 21 confounders were examined (criteria and effects) pertaining to 5 clinical endpoints: socioeconomic status, gas stove usage, other factors in family history, and subject's personal health history. An analysis of the 16 remaining confounders

## MATERIALS

The 45 clinical endpoint studies under examination correspond to the 21 potential confounders under examination. The 21 potential confounders under examination, as well as from factors that had a direct or indirect effect on the respiratory system, designated with an asterisk were considered here. The remainder are considered here.

Table 1. Potential Confounders Considered in the Analysis of Household Smoking and of School-Age and Older Children

- |  |
|--|
| 1. Socioeconomic status*                         |
| 2. Gas stove usage*                              |
| 3. Family health history*                        |
| 4. Subject's personal health history*            |
| 5. Infant feeding (breast vs. bottle)            |
| 6. Outdoor pollution                             |
| 7. Indoor pollution (other than gas stove usage) |
| 8. Day care use                                  |
| 9. Family size                                   |
| 10. Animal exposures                             |
| 11. Stress                                       |

\* Potential confounders considered in previous analyses

As described previously [7], a pre-determined set of criteria were regarded as having been fulfilled: 1) the authors were homogeneous with regard to a parental/household smoking) and



the remaining 16. This was used for several of the confounding variables: location of residence, age, dampness and cold, type of heating, type of ventilation, type of respiratory symptoms and signs (age, male gender) or (residence). With regard to endpoints and the confounding variables, either not observed, of an effect of standardization in the influence of certain of the confounding variables on the study of the respiratory clinical and children.

ed analytical review of the parental/household smoking history system of school-age or older children and 38 pulmonary function studies that had been done on children. This indicated little to no effect of this surrogate for ETS on such as prevalence of cough, pulmonary function parameters as

other factors that might co-vary. Important factors that can affect the results have suggested that this lack of control for potential confounders which potential confounders.

We have also suggested that the lack of medical records of parental or medical records of parental respiratory symptoms and signs served from study to study with

only initiated further analyses to control for confounding variables were pulmonary function endpoints. The frequency with which clinical or medical records in the study is dealt with the frequency with which frequency and consistency with

which these 21 confounders were considered, and specific details (such as criteria and effects) pertaining to 5 individual confounders, namely socioeconomic status, gas stove usage, other forms of indoor pollution, family health history, and subject's personal health history [7]. The current report deals with an analysis of the 16 remaining confounding variables.

## MATERIALS AND METHODS

The 45 clinical endpoint studies and 38 pulmonary function endpoint studies under examination correspond to those reviewed in previous reports [1-3,7-75]. The 21 potential confounders under examination (Table 1) were derived from variables considered in the papers under review and other epidemiologic studies, as well as from factors that intuitively seemed likely to have a potential direct or indirect effect on the respiratory system. As shown in Table 1, those designated with an asterisk were considered in our previous report [7], while the remainder are considered here.

Table 1. Potential Confounders Considered in Epidemiologic Studies of Parental/Household Smoking and Respiratory Health and Pulmonary Function of School-Age and Older Children.

1. Socioeconomic status*	12. Dampness and cold
2. Gas stove usage*	13. Type of heating and presence of air conditioning
3. Family health history*	14. Season
4. Subject's personal health history*	15. Occupational exposures of subject (direct or indirect)
5. Infant feeding (breast vs. bottle)	16. Quality of housing
6. Outdoor pollution	17. Nutritional status of subject
7. Indoor pollution (other than gas stove usage)*	18. Residence location
8. Day care use	19. Age of subject
9. Family size	20. Gender of subject
10. Animal exposures	21. Active smoking by subject
11. Stress	
* Potential confounders considered in previous report [7]	

As described previously [7], a protocol was employed to systematically extract relevant information from each of the studies under examination. Potential confounders were regarded as having been addressed if any one of the following criteria were fulfilled: 1) the authors of the study considered the population to be homogeneous with regard to a potential confounder; 2) the exposed (e.g. to parental/household smoking) and nonexposed subjects were said to be matched

with regard to the potential confounder; 3) statistical adjustment was made for the potential confounder; or 4) it was regarded in the study as an independent risk factor.

The following information pertaining to potential confounding variables was tabulated: 1) what criterion (or criteria) was (were) employed for each potential confounder; 2) whether a statistically significant association was looked for between a potential confounder and an endpoint and, if so, what was the direction of this association; and 3) whether there was evidence of possible interaction between the potential confounder in question and other potential confounders (including parental/household smoking) that influenced the outcome of the study. From this tabulated information, the consistency from paper to paper relative to each item was determined.

In two instances, the Park and Kim study [34, 35] and the Stern et al. study [40, 41], basically the same data, slightly updated, was reported twice. Although each of the reports is cited, for each study the two reports are considered to represent a single study in the following tabulations.

## RESULTS

Table 2. Consideration of Family Size in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease of Older Children

Published Study	Parameter	Association of Parameters
Colley, 1974 [9]	number of siblings	associated with increased respiratory symptoms
Lebowitz/Burrows, 1976 [10]	family size	none reported
Saidi et al., 1978 [12]	number of siblings	associated with decreased prevalence of adenoidectomy and tonsillectomy
Tager et al., 1979 [15]	number of persons per room comparable in exposed & nonexposed households, controlled for sibship size	NA (matched)
Weiss et al., 1980 [17]	density of persons per room	none observed for wheeze
Bonham/Wilson, 1981 [18]	number of adults in household	none observed for restricted activity due to respiratory illness of the child
Dodge, 1982 [19]	avg size of household same for exposed and nonexposed subjects	NA (matched)
Gortmaker et al., 1982 [20]	family size	none reported

Published Study	
Tashkin et al., 1984 [26]	stated evenly expos
Vogt, 1984 [27]	no. of hold
Ware et al., 1984 [28]	numb: home
Fergusson/Horwood, 1985 [29]	famil:
Horwood et al., 1985 [30]	famil:
Burchfiel et al., 1986 [32]	numt
McConnochie/Rogghmann, 1986 [33]	crow: pres:
Park/Kim, 1986, 1988 [34, 35]	num num:
Strachan/Elton, 1986 [36]	4 or othe thar:
Willat, 1986 [38]	fam:
Dijkstra et al., 1988 [44]	crow: pos
Somerville et al., 1988 [46]	nur: cro:
Angioni et al., 1989 [47]	no. san: ind
McConnochie/Rogghmann, 1989 [50]	fam: cro:
Neuspeil et al., 1989 [51]	cro:

### A. Family Size

As shown in Table 2, seven endpoint papers that considered of persons/room; number of as a dichotomized or continuous individuals occupying the subject observed association between toms and/or diseases [17, 18, 29] observing either a positive [9]

adjustment was made for study as an independent

confounding variables was employed for each potential association was looked for and, if so, what was the evidence of possible association and other potential that influenced the outcome consistency from paper

and the Stern et al. study reported twice. Although reports are considered to

Parental Household Smoking  
Older Children

Association of Parameters	
associated with increased respiratory symptoms	none reported
associated with decreased prevalence of adenoidectomy and tonsillectomy	NA (matched)
none observed for wheeze	none observed for wheeze
none observed for respiratory activity due to respiratory illness of the child	NA (matched)
none reported	none reported

Published Study	Parameter	Association of Parameter(s)
Tashkin et al., 1984 [26]	stated that family size was evenly distributed among exposure groups	NA (matched)
Vogt, 1984 [27]	no. of children in household	associated with decreased utilization of outpatient and inpatient care services at HMO
Ware et al., 1984 [28]	number of persons living in home	none reported
Fergusson/Horwood, 1985 [29]	family size	none reported
Horwood et al., 1985 [30]	family size	none observed for asthma
Burchfiel et al., 1986 [32]	number persons in household	none reported
McConnochie/Rogghmann, 1986 [33]	crowding in household; presence of older siblings	none observed for asthma and wheezing
Park/Kim, 1986, 1988 [34, 35]	number of family members; number of siblings	none observed for coughing
Strachan/Elton, 1986 [36]	4 or more persons in family; other children in family; more than 1 person/room	none observed for wheeze, cough, respiratory illness
Willat, 1986 [38]	family density no. of siblings	none observed for sore throats
Dijkstra et al., 1988 [44]	crowding of home and possession of own bedroom	none reported
Somerville et al., 1988 [46]	number of siblings; household crowding	none reported
Angioni et al., 1989 [47]	no. of people sleeping in same room as child; crowding index (no. people per room)	none observed respiratory and nonrespiratory allergies
McConnochie/Rogghmann, 1989 [50]	family size and household crowding	none observed for asthma or wheezing
Neuspeil et al., 1989 [51]	crowding in home	none observed for wheezy bronchitis

#### A. Family Size

As shown in Table 2, several criteria were variably employed in the 23 clinical endpoint papers that considered family size including: number of siblings; number of persons/room; number of adults in the household; crowding in the household as a dichotomized or continuous variable; presence of older siblings; and number of individuals occupying the subject's bedroom. Of the 23 studies, 10 reported no observed association between family size and prevalence of respiratory symptoms and/or diseases [17, 18, 30, 33, 34, 35, 36, 38, 47, 50, 51], while 3 studies reported observing either a positive [9] or a negative [12, 27] association. Three of these

studies were classified as matched [15, 19, 26] and 7 studies, designated as "not reported", provided no data pertaining to the presence or absence of an association [20, 28, 29, 32, 44, 46].

Table 3 shows that 13 pulmonary function studies employed such criteria as number of siblings, number of persons/room, and number of persons in the home as indices of family size. Seven of these studies reported no observed association between family size and pulmonary function [55, 61, 62, 63, 69, 70, 72], while three of the studies reported an observation of the existence of such an association. Five studies were classified as homogeneous or matched [15, 19, 26, 67] and 2 studies reported no data relative to this issue [28, 32].

Table 3. Consideration of Family Size in Studies of Parental/Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameters
Leeder et al., 1976 [55]	number of siblings	none observed for peak expiratory flow rate
Tager et al., 1979 [15]	number of persons per room comparable in exposed and nonexposed households, controlled for sibship size	NA (matched)
Ware et al., 1984 [28]	number of persons living in home	none reported
Hasselbad et al., 1981 [61]	density of people per room	none observed for FEV <sub>0-3</sub>
Dodge, 1982 [19]	avg size of household was same for exposed and nonexposed subjects	NA (matched)
Lebowitz et al., 1982 [62]	family size	none observed for FVC, FEV <sub>1</sub> , Vmax <sub>50</sub> , and Vmax <sub>25</sub>
Lebowitz et al., 1984 [63]	family size	none observed for family aggregation of pulmonary function
Tashkun et al., 1984 [26]	family size was evenly distributed among exposure groups	NA (matched)
Burchfiel et al., 1986 [32]	family size	none reported
Chen/Li, 1986 [67]	avg household residential area per capita similar in exposed and nonexposed subjects	NA (matched)
Evans et al., 1987 [69]	number of people in household, number of people per room	none observed for FEV <sub>1</sub>
Martinez et al., 1988 [70]	number of persons in household	none observed for bronchial responsiveness
Murray/Morrison, 1988 [72]	number of siblings	none observed for baseline pulmonary function and bronchial responsiveness in asthmatics

### B. Location of Residence

As shown in Table 4, 25 studies considered potential confounding variable in following criteria: proximity to region and definition of area as urban, suburban, or rural. Thirteen were considered to be homogeneous or matched [36, 39, 40, 41, 42, 44, 50, 52]. Four studies reported an association [14, 16, 24, 47], three reported no association [43], and four provided no relevant data suggested a possible interaction between pollution and parental/household smoking.

Table 4. Consideration of Location of Residence in Studies of Parental/Household Smoking and Pulmonary Function in Children

Published Study	Parameter
Kasuga et al., 1979 [14]	residence proximity to region
Tager et al., 1979 [15]	East European graph
Speizer et al., 1980 [16]	Harvard (12 cities)
Weiss et al., 1980 [17]	East European graph
Dodge, 1982 [19]	non-smoking size pressure
Gortmaker et al., 1982 [20]	urban (Be sur)
Rantakallio, 1983 [22]	plavil
Schenker et al., 1983 [23]	are pr
Charlton, 1984 [24]	in re

s, designated as "none  
ence of an association [10,

employed such criteria as  
of persons in the home  
1 no observed association  
3, 69, 70, 72], while none  
such an association. Four  
19, 26, 67] and 2 studies

ntal/Household Smoking

## B. Location of Residence

As shown in Table 4, 25 studies that considered location of residence as a potential confounding variable in clinical endpoint studies variably used the following criteria: proximity to region of pollution; geographically defined area; and definition of area as urban, suburban, nonurban, and rural. Of these studies, 13 were considered to be homogeneous or matched [15, 17, 29, 30, 33, 34, 35, 36, 39, 40, 41, 42, 44, 50, 52]. Four of these studies reported no observed association [14, 16, 24, 47], three reported observing an association [19, 20, 31, 43], and four provided no relevant information [22, 23, 28, 54]. In one study, the data suggested a possible interaction between location of residence, outdoor pollution and parental/household smoking [14].

Table 4. Consideration of Location of Residence in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter	Association of Parameter(s)
Kasuga et al., 1979 [14]	residential area within Tokyo, proximity to highway	see Table 12 B none observed for this parameter alone
Tager et al., 1979 [15]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Speizer et al., 1980 [16]	Harvard Six Cities Study (12 separate cohorts from 6 cities)	none observed for respiratory illness before 2 years of age (not reported for other endpoints)
Weiss et al., 1980 [17]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Dodge, 1982 [19]	non-urban, all subjects from 3 small communities ranging in size from 4000 to 7312 people; presence or absence of copper smelters within community	see Table 12 B
Gortmaker et al., 1982 [20]	urban (Flint, Mich.) and rural (Berkshire, Mass.) from 2 separate survey populations	urban area associated with increased incidence of asthma
Rantakallio, 1983 [22]	place of residence (town-village-remote, village)	none reported
Schenker et al., 1983 [23]	area predominantly rural, proximity to industrial pollution	see Table 12 B
Charlton, 1984 [24]	industrial vs. non-industrial regions	none observed for prevalence of cough

Association of Parameter(s)
none observed for peak expiratory flow rate
NA (matched)
reported
observed for FEV <sub>0-1</sub>
NA (matched)
none observed for FVC, FEV <sub>1</sub> , Vmax <sub>50</sub> , and Vmax <sub>25</sub>
none observed for family aggregation of pulmonary function
NA (matched)
none reported
NA (matched)
none observed for FEV <sub>1</sub>
none observed for bronchial responsiveness
none observed for bronchial pulmonary function and for responsiveness in asthma

Published Study	Parameter	Association of Parameter
Ware et al., 1984 [28]	Harvard Six Cities Study (6 locations with range of outdoor air qualities); adjustment as "city-cohort" in multiple logistic regression	none reported
Fergusson/Horwood, 1985 [29]	urban region of Christchurch, New Zealand	NA (homogeneous)
Horwood et al., 1985 [30]	urban region of Christchurch, New Zealand	NA (homogeneous)
Spinaci et al., 1985 [31]	3 geographic areas within Turin, Italy	see Table 12 B
McConnochie/Roghmann, 1986 [33]	suburban Rochester, N.Y.	NA (homogeneous)
Park/Kim, 1986, 1988 [34, 35]	rural (Korea)	NA (homogeneous)
Strachan/Elton, 1986 [36]	urban area of Edinburgh, Scotland	NA (homogeneous)
O'Connor et al., 1987 [39]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Stem et al., 1987, 1989 [40, 41]	all locations rural Canada but adjustment for city of residence	see Table 12 B
Tsimoyianis et al., 1987 [42]	suburban Nassau County, New York	NA (homogeneous)
Andrae et al., 1988 [43]	7 rural areas, 2 of the areas compared on the basis of proximity to pulp and paper plant	proximity to pulp and paper plant associated with increased bronchial hyperactivity and allergic disease;
Dijkstra et al., 1988 [44]	rural area of southeast Netherlands	NA (homogeneous)
Angioni et al., 1989 [47]	home in inner city, suburb, and country	none observed for allergic respiratory and nonrespiratory disease
Charlton/Blair, 1989 [54]	school area	none reported
McConnochie/Roghmann, 1989 [50]	suburban Rochester, N.Y.	NA (homogeneous)
Sherman et al., 1990 [52]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)

Location of residence (geographically defined area, proximity to source of outdoor pollution, and definition of area as urban, suburban, and rural) was considered in 20 pulmonary function endpoint studies and is detailed in Table 5. Eleven of these studies were classified as homogeneous or matched [55, 57, 15, 17, 58, 59, 39, 67, 69, 42, 44]. One study reported no observed association

[59] and four studies reported no association of pulmonary function [16, 60, 61, 62] regarding location of residence

Table 5. Consideration of Location of Residence, Smoking and Pulmonary Function

Published Study	Parameter
Leeder et al., 1976 [55]	Harvard Six Cities Study
Tager et al., 1976 [57]	East Boston, Mass.
Tager et al., 1979 [15]	East Boston, Mass.
Weiss et al., 1980 [17]	East Boston, Mass.
Tager et al., 1983 [58]	East Boston, Mass.
Tager et al., 1985 [59]	East Boston, Mass.
O'Connor et al., 1987 [39]	East Boston, Mass.
Speizer et al., 1980 [16]	Harvard Six Cities Study
Ware et al., 1984 [28]	Harvard Six Cities Study
Berkey et al., 1986 [60]	Harvard Six Cities Study
Hasselbad et al., 1981 [61]	Harvard Six Cities Study
Dodge, 1982 [19]	Harvard Six Cities Study

Association of Parameter(s)
none reported
NA (homogeneous)
NA (homogeneous)
see Table 12 B
NA (homogeneous)
NA (homogeneous)
NA (homogeneous)
NA (homogeneous)
see Table 12 B
NA (homogeneous)
proximity to pulp and paper mill associated with increased bronchial hyperactivity and allergic disease.
NA (homogeneous)
none observed for allergic respiratory and nonrespiratory disease
none reported
NA (homogeneous)
NA (homogeneous)

area, proximity to source of pollution, suburban, and rural. Studies and is detailed in Table 12. In homogeneous or matched case-control studies, no observed association.

[19] and four studies reported that location of residence was associated with level of pulmonary function [16, 60, 61, 31]. Four studies provided no information regarding location of residence and pulmonary function [28, 26, 40, 41, 74].

Table 5. Consideration of Location of Residence in Studies of Parental/Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameter(s)
Leeder et al., 1976 [55]	Harrow, a residential suburb of NW London	NA (homogeneous)
Tager et al., 1976 [57]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al., 1979 [15]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Weiss et al., 1980 [17]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al., 1983 [58]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al., 1985 [59]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
O'Connor et al., 1987 [39]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Speizer et al., 1980 [16]	Harvard Six Cities Study (12 separate cohorts from 6 cities); adjustment for cohort (including both location and year of study)	cohort was associated with FEV <sub>1</sub> and FVC, indicating differences from city to city and year to year in these parameters
Ware et al., 1984 [28]	Harvard Six Cities Study (6 locations with range of outdoor air qualities); adjustment as "city-cohort" in multiple logistic regression	none reported
Berkey et al., 1986 [60]	Harvard Six Cities Study (corrected for 6 separate locales)	some geographic differences observed in level and growth rates of FVC and FEV <sub>1</sub>
Hasselbad et al., 1981 [61]	33 communities from 7 metropolitan areas in different geographic locations in US; considered in analysis of covariance	accounted for the greatest amount of variation in mean FEV <sub>0.75</sub> ; see also table 13 B
Judge, 1982 [19]	non-urban; all subjects from 3 small communities ranging in size from 4000 to 7312 people; presence or absence of copper smelters within community	see Table 13 B none observed

Published Study	Parameter	Association of Parameter
Tashkin et al., 1984 [26]	4 selected areas of Los Angeles County (adjusted for)	none reported
Spinaci et al., 1985 [31]	3 geographic areas (central urban (UC), peripheral (UP) and suburban (SU)) within Turin, Italy	see Table 13 B
Chen/Li, 1986 [67]	urban district of Shanghai	NA (homogeneous)
Evans et al., 1987 [69]	urban, 4 hospitals in New York City	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all locations, rural Canada; adjusted for city of residence	none reported
Tsimoyianis et al., 1987 [42]	suburban Nassau County, New York	NA (homogeneous)
Dijkstra et al., 1988 [44]	rural area of southeast Netherlands	NA (homogeneous)
Kauffmann et al., 1989 [74]	24 areas in 7 French cities; adjusted for town of residence	none reported

### C. Age of the Subject

Table 6. Consideration of Age of Subject in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter (ages)	Association of Parameter(s)
Cameron et al., 1969 [8]	5 or less vs. 9 or less vs. 16 or less (5 or less -16)	household smoke exposure associated with increased respiratory illness 16 or less not in other age groups
Colley, 1974 [9]	age of child (6-14)	none reported
Lebowitz/Burrows, 1976 [10]	age of child (under 15)	none reported
Schilling et al., 1977 [11]	7-15 yrs of age vs. 15-18 (7-18)	prevalence of wheeze in children associated with parental wheeze in younger children (numbers may be inadequate in older children)
Said et al., 1978 [12]	above and below 15 years of age (10-20)	none observed for adenoidectomy or tonsillectomy
Bland et al., 1978 [13]	all children in 1st yr of secondary school (not given)	NA (homogeneous)
Kasuga et al., 1979 [14]	none (6-11)	NA
Tager et al., 1979 [15]	none (5-9)	NA

Published Study	P
Speizer et al., 1980 [16]	a
Weiss et al., 1980 [17]	r
Bonham/Wilson, 1981 [18]	t
Dodge, 1982 [19]	
Gortmaker et al., 1982 [20]	
Ekwo et al., 1983 [21]	
Rantakallio, 1983 [22]	
Schenker et al., 1983 [23]	
Charlton, 1984 [24]	
Lebowitz, 1984 [25]	
Tashkin et al., 1984 [26]	
Vogt, 1984 [27]	
Ware et al., 1984 [28]	
Fergusson/Horwood, 1985 [29]	
Horwood et al., 1985 [30]	
Spinaci et al., 1985 [31]	



Association of Parameter(s)
none reported
see Table 13 B
NA (homogeneous)
NA (homogeneous)
none reported
NA (homogeneous)
NA (homogeneous)
none reported

# Effects of Parental/Household Disease in Older Children

Association of Parameter(s)
household smoke exposure associated with increased respiratory illness 16 or less not in other age groups
none reported
none reported
prevalence of wheeze in children associated with parental wheeze in younger children (numbers may be inadequate in older children)
none observed for adenoid ectomy or tonsillectomy
NA (homogeneous)
NA
NA

Published Study	Parameter	Association of Parameter(s)
Speizer et al., 1980 [16]	age at time of reporting (6-10)	none observed for infant respiratory disease
Weiss et al., 1980 [17]	none (4-10)	NA
Bonham/Wilson, 1981 [18]	under 6 vs. 6-11 vs. 12-16 yr (0-16)	none observed for restricted activity due to acute respiratory conditions
Dodge, 1982 [19]	subjects were 3rd and 4th grade children at inception of the 4 yr longitudinal study (8-12)	NA (homogeneous)
Gortmaker et al., 1982 [20]	above and below 5 yrs of age (0-17)	none observed for asthma
Ekwo et al., 1983 [21]	none (6-12)	NA
Rantakallio, 1983 [22]	all subjects were the same age (14)	NA (homogeneous)
Schenker et al., 1983 [23]	5-9 yrs vs 10-14 years (5-14)	respiratory symptoms (cough, phlegm, wheeze) and chest illness more prevalent in younger children
Charlton, 1984 [24]	<11, 11-13, >14 yrs of age (8-19)	prevalence of cough decreased with increasing age
Lebowitz, 1984 [25]	none (4-24)	NA
Tashkin et al., 1984 [26]	age of child (7-17)	none reported
Vogt, 1984 [27]	age of child (0-5 vs. 6-11 vs. 12-18 yrs) (0-18)	as child ages outpatient service utilization (primarily for upper respiratory infec- tion), as well as inpatient care, declines
Ware et al., 1984 [28]	age of children (6-10)	prevalence of respiratory illnesses higher in younger children
Fergusson/Horwood, 1985 [29]	birth cohort compared at intervals of 2yrs (0-6)	prevalence of respiratory symptoms and illness decreases as age of the child increases; association with maternal smoking disappears after 2 years of age
Horwood et al., 1985 [30]	birth cohort compared at yearly intervals (0-6)	cumulative rates of asthma (per 100 children) increased with age as the number of risk factors increased
Spencer et al., 1985 [31]	age of child (11)*	none reported

Published Study	Parameter	Association of Parameters
Burchfiel et al., 1986 [32]	0-4yr vs. 9yr vs. 10-14yr vs. 15-19 yr (0-19)	prevalence of phlegm, asthma and chest colds tend to increase as age increases but asthma not statistically significant; no consistent age association for cough, asthma, and bronchitis
McConnochie/Rogghmann, 1986 [33]	mean age 8.4 yr (6-10)	NA (homogeneous)
Park/Kim, 1986, 1988 [34, 35]	child's age (under 5 vs. 6-11 vs. 12-14 yr) (0-14)	incidence coughing decreased with increasing age
Strachan/Elton, 1986 [36]	children approximately the same age (7-8)	NA (homogeneous)
Teculescu et al., 1986 [37]	exposed child matched for age with nonexposed child (10-16)	NA (matched)
Willat, 1986 [38]	age of child (2-15)	older children had a higher prevalence of sore throats
O'Connor et al., 1987 [39]	age of subjects matched for exposed and nonexposed non-asthmatic and asthmatic subjects (6-21)	NA (matched)
Stern et al., 1987, 1989 [40, 41]	none (7-12)	NA
Tsumoyianis et al., 1987 [42]	exposed and nonexposed matched for age (12-17)	NA (matched)
Andrae et al., 1988 [43]	6 mos-7 yr vs 8-16 yr (0.5-16)	outdoor pollution associated with increased incidence of asthma and coughing in older group of children; none reported
Dijkstra et al., 1988 [44]	age of child (6-12)	NA
Moreno et al., 1988 [45]	none (8-13)	NA
Somerville et al., 1988 [46]	none (5-11)	NA
Angoni et al., 1989 [47]	age of subject (6,7,8,9,10, and 10+ yr) (6-10+)	none observed for respiratory and nonrespiratory allergic disease
Berwick et al., 1989 [48]	above and below 7 yrs of age (5-13)	children below age of 7 yr exhibit increased incidence lower respiratory symptoms when exposed to 30 ug/m <sup>3</sup>
NO <sub>2</sub>		
Chan et al., 1989 [49]	all children same age (7)	NA (homogeneous)
Charlton/Blair, 1989 [54]	all children same age (12-13)	NA (homogeneous)

Published Study	Parameter
McConnochie/Rogghmann, 1989 [50]	cc 8 (C)
Neuspeil et al., 1989 [51]	b sc
Sherman et al., 1990 [52]	b a
Strachan et al., 1990 [53]	a
Average age	

As shown in Table 6, a wide range of ages were employed in the 45 clinical studies. 38 studies attempted to control for age as a variable. In 12 of these studies, the subjects were homogeneous or matched for age. In 12 studies, the subjects were matched for age and clinical endpoints [12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23]. In 12 studies, the subjects were matched for age and clinical endpoints [12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23]. In 12 studies, the subjects were matched for age and clinical endpoints [12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23].

As in the case of the clinical studies, comparisons and age range were considered age of the subjects. The majority of these studies reported no observed association for age in 10 studies [55, 56, 57, 58, 59, 60, 61, 62, 63, 64]. Several studies suggested other factors with regard to parental/household smoking, gender [64, 66] and subject's age provided no direct information on pulmonary function [65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100].

Association of Parameter(s)
prevalence of phlegm, wheeze, and chest colds tend to decrease as age increases but generally not statistically significant; no consistent age association for cough, asthma, and bronchitis
NA (homogeneous)
incidence coughing decreased with increasing age.
NA (homogeneous)
NA (matched)
older children had a higher prevalence of sore throats
NA (matched)
(matched)
outdoor pollution associated with increased incidence of asthma and coughing in older group of children none reported
NA
NA
none observed for respiratory and nonrespiratory allergic disease
children below age of 7 exhibit increased incidence lower respiratory symptoms when exposed to 30 ug m <sup>-3</sup>
NA (homogeneous)
NA (homogeneous)

Published Study	Parameter	Association of Parameter(s)
McConnochie/Rogghmann, 1989 [50]	cohort examined at mean age 8 yrs with mean age 13 yrs (6-10 and 11-15)	bronchiolitis history is a risk factor for wheeze and asthma at age 8 but not 13 yrs
Neuspeil et al., 1989 [51]	birth cohort examined at same age (10 yrs)	NA (homogeneous)
Sherman et al., 1990 [52]	below and above 10 years of age (5-22)	none observed for first occurrence of asthma
Strachan et al., 1990 [53]	all children same age (6.5-7.5)	NA (homogeneous)
Average age		

As shown in Table 6, a wide variety of age comparisons and age ranges were employed in the 45 clinical endpoint studies pertaining to household/parental smoking. 38 studies attempted to control for age of the subjects as a confounding variable. In 12 of these studies, age of the subject was considered either to be homogeneous or matched [13, 19, 22, 33, 36, 37, 39, 42, 49, 54, 51, 53]. Seven studies reported no significant observed association between age of the subject and clinical endpoints [12, 16, 18, 20, 32, 47, 52]. Nine of the studies indicated that the prevalence of respiratory symptoms and illness decreased as the child got older within a study population [11, 23, 24, 27, 28, 29, 34, 35, 48, 50]. Several studies suggested an interaction between age of the subject and other variables, such as household smoke exposure [8], family history [11], indoor pollution [48] and subject's health history [50]. Three studies reported observing a converse association, i.e., that risk of respiratory illness increased with age of the subject [30, 38, 43]. Five of these studies [9, 10, 26, 31, 44] provided no information regarding any association between age of the subject and clinical endpoints.

As in the case of the clinical endpoint studies, there were a variety of age comparisons and age ranges in the 37 pulmonary function endpoint studies that considered age of the subject as a potential confounding variable, although in the majority of these studies this involved an age adjustment relative to pulmonary function (Table 7). Pulmonary function was matched or homogeneous for age in 10 studies [55, 56, 39, 68, 37, 42, 70, 72, 73, 53]. None of the studies reported no observed association. 12 studies reported an association between age and some parameter of pulmonary function [11, 58, 59, 60, 61, 19, 64, 26, 66, 32, 67, 74] that indicated increases in the level of performance as the child aged. Several studies suggested interactions between age of the subject and other factors with regard to pulmonary function, such as active smoking [59, 64], parental/household smoking [64, 75], gender and maternal smoking [61, 26, 71], gender [64, 66] and subject's personal health history [64]. Sixteen studies provided no direct information on any association between age of the subject and pulmonary function [57, 15, 17, 16, 28, 21, 62, 25, 63, 65, 31, 40, 41, 44, 69, 71, 75].

Table 7. Consideration of Age of Subject in Studies of Parental Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter (ages)	Association of Parameter
Leeder et al., 1976 [55]	all children: same age (5)	NA (homogeneous)
Schilling et al., 1977 [11]	adjusted for age; age considered in multiple regression analysis (7-18)	age (as well as weight and height) major contributor to variance
Yarnell/St. Leger, 1979 [56]	none (7-18)	NA
Tager et al., 1976 [57]	adjusted for age (5-31)	none reported
Tager et al., 1979 [15]	adjusted for age (5-19)	none reported
Weiss et al., 1980 [17]	adjusted for age (5-10)	none reported
Tager et al., 1983 [58]	adjusted for age; age considered in autoregressive model (4-28)	age of subject had negative influence on change in FEV <sub>1</sub> over a one year period
Tager et al., 1985 [59]	adjusted for age; age considered in autoregressive model (5-19)	age-dependent FEV <sub>1</sub> growth curve is sigmoid between 5-20 years; decrement in FEV <sub>1</sub> and FEV <sub>25-75</sub> associated with smoking most pronounced in older children (>15 yrs)
O'Connor et al., 1987 [39]	age of subjects not significantly different for exposed and nonexposed (as well as asthmatic and nonasthmatic) subjects (6-21)	NA (matched)
Speizer et al., 1980 [16]	adjusted for age (6-10)	none reported
Ware et al., 1984 [28]	adjusted for age (6-9)	none reported
Berkey et al., 1986 [60]	adjusted for age (6-10)	unadjusted FEV <sub>1</sub> and FVC increase with age from 6-10 years
Hasselbad et al., 1981 [61]	function adjusted for age; compared at 6-9 vs. 9-13 yrs (6-13)	FEV <sub>0.75</sub> increased in older children; according to authors maternal smoking produced a larger decrement in FEV <sub>0.75</sub> of older boys than younger boys and older and younger girls
Dodge, 1982 [19]	subjects were 3rd and 4th grade children at inception of this 4 year longitudinal study; lung growth adjusted for age of subject (8-12)	FEV <sub>1</sub> increases as child ages

Published Study	Parameter
Ekwo et al., 1983 [21]	age of regress
Lebowitz et al., 1982 [62]	adjust
Lebowitz, 1984 [25]	adjust
Lebowitz et al., 1984 [63]	adjust
Lebowitz et al., 1987 [64]	age of regress
Lebowitz/Holberg, 1987 [65]	adj
Tashkin et al., 1984 [26]	adj. con. 17
Vedal et al., 1984 [66]	ad
Spinaci et al., 1985 [31]	ag
Burchfiel et al., 1986 [32]	as ft 1

of Parental/Household  
Children

Association of Parameter(s)
NA (homogeneous)
age (as well as weight and height) major contributor to variance
NA
none reported
none reported
none reported
age of subject had negative influence on change in FEV <sub>1</sub> over a one year period
age-dependent FEV <sub>1</sub> growth curve is sigmoid between 5-20 years; decrement in FEV <sub>1</sub> and FEV <sub>25-75</sub> associated with smoking most pronounced in older children (>15 yrs)
N matched)
none reported
none reported
unadjusted FEV <sub>1</sub> and FVC increase with age from 6-17 years
FEV <sub>0.75</sub> increased in older children; according to authors maternal smoking produced a larger decrement in FEV <sub>1</sub> of older boys than younger boys and older and younger girls
FEV <sub>1</sub> increases as child ages

Published Study	Parameter (ages)	Association of Parameter(s)
Ekwo et al., 1983 [21]	age of child considered in regression analysis (6-12)	none reported
Lebowitz et al., 1982 [62]	adjusted for age (>6)	none reported
Lebowitz, 1984 [25]	adjusted for age (4-24)	none reported
Lebowitz et al., 1984 [63]	adjusted for age (13-5)	none reported
Lebowitz et al., 1987 [64]	age of child considered in regression analysis (5.5-25)	FEV <sub>1</sub> exhibits curvilinear relationship with age and height together; age-sex interaction exhibited for Vmax <sub>50</sub> /FVC (higher in females aged 13-25 yr); history of AOD associated with age-dependent loss of Vmax <sub>50</sub> ; earlier onset of asthma (<5 yr) associated with greater decrements in Vmax <sub>50</sub> ; maternal smoking associated with significantly increased FVC in older age groups; smoking associated with greater decrements of function of older (15-25yr) subjects
Lebowitz/Holberg, 1987 [65]	adjusted for age (5.5-25)	none reported
Tashkin et al., 1984 [26]	adjusted for age; function compared at 7-11 vs 12-17 yr (7-17)	pulmonary function elevated in older group of males and females; maternal smoking associated with decreases of selected functional parameters in younger males (Vmax, V <sub>25</sub> , V <sub>50</sub> ) and older females (FEV <sub>25-75</sub> , V <sub>50</sub> , V <sub>75</sub> )
Vedal et al., 1984 [66]	adjusted for age (5-14)	age was a predictor of all functional measures (FVC, FEV <sub>0.75</sub> , FEV <sub>25-75</sub> , Vmax <sub>50</sub> , Vmax <sub>75</sub> ); a significant interaction found between age and sex for all measures except FVC (flow rates increased in girls with age relative to boys)
Spinaci et al., 1985 [31]	age of subject (11)	none reported
Burchfiel et al., 1986 [32]	adjusted for age; compared function at 10-14 vs. 15-19 yrs (10-19)	older group of children had higher levels of FEV <sub>1</sub> , FVC, Vmax <sub>50</sub>

Published Study	Parameter (ages)	Association of Parameter
Chen/Li, 1986 [67]	age of child considered as a variable in regression analysis (8-16)	FVC associated with age; none reported for FEV <sub>1</sub> , MMEF, FEF <sub>25-75</sub>
Murray/Morrison, 1986 [68]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age (7-17)	NA (matched)
Teculescu et al., 1986 [37]	exposed and nonexposed subjects matched for age (10-16)	NA (matched)
Evans et al., 1987 [69]	age of child considered in multiple regression analysis (4-17)	none reported
Stern et al., 1987, 1989 [40, 41]	adjusted for age (7-12)	none reported
Tsimoyianis et al., 1987 [42]	exposed and nonexposed subjects matched for age (12-17)	NA (matched)
Dijkstra et al., 1988 [44]	adjusted for age (6-12)	none reported
Martinez et al., 1988 [70]	all children same age (9)	NA (homogeneous)
Masi et al., 1988 [71]	age of subject considered in regression analysis (13-36)	duration of ETS exposure at home (persons X years) associated decreased FEF <sub>25-75</sub> and Vmax <sub>25</sub> in males. ETS expo-in men before 17 years of age associated with decreased FEF <sub>25-75</sub>
Murray/Morrison, 1988 [72]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age (7-17)	NA (matched)
Chan et al., 1989 [73]	all children same age (7)	NA (homogeneous)
Kauffmann et al., 1989 [74]	adjusted for age	(6-10) age related patterns of FEV <sub>1</sub> and FEF <sub>25-75</sub> observed
Murray/Morrison, 1989 [75]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age, compared function at 7-11, and 12-17 yrs (7-17)	in older age group maternal smoking associated with decreased FEV <sub>1</sub> , FEF <sub>25-75</sub> , and PC <sub>20</sub> , not FVC
Strachan et al., 1990 [53]	all children same age (6.5-7.5)	NA (homogeneous)
Average age		

### E. Gender of Subject

As shown in Table 8, 32 clinical endpoint studies considered gender of subject as a confounding variable. Of these, 2 studies were matched for gender [8, 39].

Ten studies reported no observed association between gender and clinical endpoints [13, 15, 17, 20, 24, 25, 26, 27, 28, 29], that the prevalence of some respiratory endpoints exceeded that in females [11, 12, 16, 30], one study reported that the prevalence of asthma predominated in females [11]. The relationship between gender and parental smoking endpoint was observed only in children where there was no consistency as to whether male or female. One study also suggested that parental history of asthma and atopy pertained to any association between gender and respiratory endpoints [44, 45].

Table 8. Consideration of Gender of Subject in Household Smoking and Children

Published Study	Parameter
Cameron et al., 1969 [8]	no significant difference in exposure
Schilling et al., 1977 [11]	gender
Said et al., 1978 [12]	gender
Bland et al., 1978 [13]	gender
Tager et al., 1979 [15]	gender
Speizer et al., 1980 [16]	gender
Weiss et al., 1980 [17]	gender

Association of Parameter(s)	
	FVC associated with age; none reported for FEV <sub>1</sub> , MMEF, FEF <sub>62-75</sub> , 30
	NA (matched)
	NA (matched)
	none reported
	none reported
	NA (matched)
	none reported
	NA (homogeneous)
	duration of ETS exposure at home (persons X years) associated decreased FEF <sub>25-75</sub> and Vmax <sub>50</sub> in males; ETS expo-in men before 17 years of age associated with decreased FEF <sub>25-75</sub>
	NA (matched)
	NA (homogeneous)
	(6-10) age related patterns of FEV <sub>1</sub> and FEF <sub>25-75</sub> observed
	in older age group maternal smoking associated with decreased FEV <sub>1</sub> , FEF <sub>25-75</sub> and PC <sub>20</sub> , not FVC
	NA (homogeneous)

Ten studies reported no observed association between gender of the subject and clinical endpoints [13, 15, 17, 20, 24, 26, 27, 38, 47, 49]. Fourteen studies reported that the prevalence of some respiratory symptoms and/or diseases in males exceeded that in females [11, 12, 16, 23, 28, 30, 31, 32, 33, 46, 54, 50, 51, 52], while one study reported that the prevalence of certain respiratory conditions predominated in females [11]. The results of four studies suggested an interaction between gender and parental smoking, whereby the association with a particular endpoint was observed only in children of one sex [13, 32, 37, 42]. However, there was no consistency as to whether the gender affected in these studies was male or female. One study also suggested an interaction between gender and parental history of asthma and atopy [52]. Four studies provided no information pertaining to any association between clinical endpoints and gender [29, 34, 35, 44, 45].

Table 8. Consideration of Gender of the Subject in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter	Association of Parameter(s)
Cameron et al., 1969 [8]	no significant gender difference in exposed vs. non-exposed	NA (matched)
Schilling et al., 1977 [11]	gender	association between a particular parental illness (bronchitis, pneumonia, and asthma) and wheeze in children influenced by gender of the child
Said et al., 1978 [12]	gender	adenoidectomy or tonsillectomy in boys > girls
Bland et al., 1978 [13]	gender	no gender differences observed for cough and breathlessness, parental smoking associated with morning cough in girls not boys
Tager et al., 1979 [15]	gender	none observed for respiratory illness and isolated cough
Speizer et al., 1980 [16]	gender	respiratory disease in males > females
Weiss et al., 1980 [17]	gender	none observed for acute respiratory illnesses (croup, bronchiolitis, bronchitis, pneumonia), atopy (hay fever, asthma), and chronic symptoms (cough/phlegm, symptoms)

Studies considered gender of subject were matched for gender

*ETS Exposure, Confounding Variables and Respiratory Health in Children:*

Published Study	Parameter (ages)	Association of Parameter
Gortmaker et al., 1982 [20]	gender considered in logistic regression analysis	none observed for asthma
Schenker et al., 1983 [23]	gender considered in multiple logistic regression	male gender risk factor for cough/phlegm, wheeze, and asthma
Charlton, 1984 [24]	gender	none observed for cough
Tashkun et al., 1984 [26]	gender	none observed for respiratory symptoms
Vogt, 1984 [27]	gender considered in multiple regression	none observed for inpatient and outpatient care
Ware et al., 1984 [28]	gender	boys had higher respiratory illness and symptom than girls
Fergusson/Horwood, 1985 [29] Horwood et al., 1985 [30]	adjusted for gender gender	none reported prevalence of asthma in boys>girls; risk factors for asthma in boys>girls
Spinaci et al., 1985 [31]	gender	prevalence of wheezing, shortness of breath and asthma in boys>girls
Burchfiel et al., 1986 [32]	gender	prevalence of phlegm, wheeze, asthma, and chest colds greater in males than females (at least in one of the age groups tested); gender differences in conditions associated with parental smoking (phlegm, wheeze, asthma, chest colds in males vs. wheeze, bronchitis, chest colds in females)
McConnochie/Roghamann 1986 [33]	gender considered in bivariate and multivariate analyses	male sex associated with wheeze but not asthma in children aged 6-10 yrs
Park/Kim, 1986, 1988 [34, 35]	gender considered in multiple logistic regression	none reported
Teculescu et al., 1986 [37]	each subject matched for gender	association between parental smoking and cough primarily in boys
Willat, 1986 [38]	gender	none observed for sore throat
O'Connor et al., 1987 [39]	gender of subjects not significantly different for exposed and nonexposed non-asthmatic and asthmatic subjects	NA (matched)

*ETS Exposure, Confounding Variables and Respiratory Health in Children:*

Published Study	Parameter
Tsamoyianis et al. 1987 [42]	gender
Dijkstra et al., 1988 [44]	ORs adjusted for gender
Moreno et al., 1988 [45]	gender
Somerville et al., 1988 [46]	gender
Angioni et al., 1989 [47]	gender
Chan et al., 1989 [49]	gender
Charlton/Blair, 1989 [54]	gender
McConnochie/Roghamann, 1989 [50]	gender and m
Neuspeil et al., 1989 [51]	gender: logistic
Sherman et al., 1990 [52]	gender: analysis

Table 9 shows that 36 of considered gender. In the majority of certain analyses, adjusted for gender [65] and 2 studies were compared pulmonary function levels of some parameters in reported higher levels of certain although reporting that gender specific information [73].



Association of Parameter(s)
none observed for asthma
male gender risk factor for cough, phlegm, wheeze, and asthma
none observed for cough
none observed for respiratory symptoms
none observed for inpatient and outpatient care
boys had higher respiratory illness and symptom than girls
none reported prevalence of asthma in boys>girls; risk factors for asthma in boys>girls
prevalence of wheezing, shortness of breath and asthma in boys>girls
absence of phlegm, wheeze, asthma, and chest colds greater in males than females (at least in one of the age groups tested); gender differences in conditions associated with parental smoking (phlegm, wheeze, asthma, chest colds in males vs. wheeze, bronchitis, chest colds in females)
male sex associated with wheeze but not asthma in children aged 6-10 yrs
none reported
association between parental smoking and cough pneumonia in boys
none observed for sore throat
NA (matched)

Published Study	Parameter (ages)	Association of Parameter(s)
Tsumoyianis et al. 1987 [42]	gender	association between ETS exposure and abnormal FEF <sub>25-75</sub> or cough statistically significant in girls but not boys
Dijkstra et al., 1988 [44]	ORs adjusted for gender	none reported
Moreno et al., 1988 [45]	gender	none reported
Somerville et al., 1988 [46]	gender	prevalence of wheezing, bronchitis, asthma, and cough in boys > girls
Angioni et al., 1989 [47]	gender	none observed for respiratory and nonrespiratory allergies
Chan et al., 1989 [49]	gender	none observed for wheeze and cough
Charlton/Blair, 1989 [54]	gender	absence from school in boys > girls
McConnochie/Roghamann, 1989 [50]	gender considered in crude and multivariate analyses	male sex associated with wheezing and asthma at age 13
Neuspeil et al., 1989 [51]	gender considered in multiple logistic regression	male sex associated with wheezy bronchitis
Sherman et al., 1990 [52]	gender considered in various analyses	male sex associated with asthma; parental asthma and atopy increased risk of asthma in females not males; history of pneumonia, bronchitis, hay fever, or sinusitis exhibited no gender difference as risk factor for asthma

Table 9 shows that 36 of the 38 pulmonary function endpoint studies considered gender. In the majority of these, pulmonary function was, at least in certain analyses, adjusted for sex. One study observed no association for gender [65] and 2 studies were matched for gender [68, 72]. Of 11 studies that compared pulmonary function on the basis of gender, eight reported higher levels of some parameters in males [55, 58, 60, 61, 26, 66, 32, 74], two studies reported higher levels of certain parameters in females [64, 66] and one study, although reporting that gender affected pulmonary performance, provided little specific information [73].

Table 9. Consideration of Gender of the Subject in Studies of Parental Household Smoking and Pulmonary Function in Older Children.

Published Study	Parameter	Association of Parameters
Leeder et al., 1976 [55]	adjusted for gender	peak expiratory flow rates: boys > girls by multiple logistic regression
Schilling et al., 1977 [11]	gender	association between family history of asthma and pulmonary function affected by gender (i.e., particular functional parameters involved); maternal smoking associated with decreased $MEF_{50\%}$ (not $FEV_1$ , $PEFR$ ) in girls, no association in boys
Yarnell/St. Leger, 1979 [56]	gender	maternal smoking associated with decrease in $FMF$ and $FEV_{0.75}$ in girls not boys
Tager et al., 1976 [57]	adjusted for gender	association between maternal smoking and decreased $FEV_1$ in boys but not girls; parent-child correlations for $FEV_1$ for girls not boys
Tager et al., 1979 [15]	adjusted for gender	none reported
Weiss et al., 1980 [17]	adjusted for gender	none reported
Tager et al., 1983 [58]	adjusted for gender; gender considered in autoregressive model	male gender has positive influence on change in $FEV_1$ over a one year period
Tager et al., 1985 [59]	adjusted for gender; gender considered in autoregressive model	decrement in $FEV_1$ associated with smoking in males > females
O'Connor et al., 1987 [39]	adjusted for gender	none reported
Ware et al., 1984 [28]	adjusted for gender	none reported; no observed influence on maternal smoking association with pulmonary function
Berkey et al., 1986 [60]	adjusted for gender	unadjusted $FEV_1$ and $FVC$ of boys > girls between 6-10 yrs of age

Published Study	Parameter
Hasselblad et al., 1981 [61]	gender
Ekwo et al., 1983 [21]	gender
Lebowitz et al., 1982 [62]	adjusted f
Lebowitz, 1984 [25]	adjusted f
Lebowitz et al., 1984 [63]	adjusted f
Lebowitz et al., 1987 [64]	gender
Lebowitz/Holberg, 1987 [65]	gender
Tashkin et al., 1984 [26]	gender
Vedal et al., 1984 [66]	adjusted

Effect in Studies of Parental/  
Action in Older Children

Association of Parameter(s)	Published Study	Parameter (ages)	Association of Parameter(s)
peak expiratory flow rates of boys > girls by multiple logistic regression	Hasselblad et al., 1981 [61]	gender	FEV <sub>0.75</sub> of boys > girls 6-13 yrs of age; maternal smoking associated with greater decrements in FEV <sub>0.75</sub> in boys than in girls; gas stove usage was associated with decreased FEV <sub>0.75</sub> in girls not in boys
association between family history of asthma and pulmonary function affected by gender (i.e., particular functional parameters involved); maternal smoking associated with decreased MEF <sub>50%</sub> (not FEV <sub>1</sub> , PEFR) in girls, no association in boys	Ekwo et al., 1983 [21]	gender	none reported
maternal smoking associated with decrease in FMF and FEV <sub>0.75</sub> in girls not boys	Lebowitz et al., 1982 [62]	adjusted for gender	none reported
association between maternal smoking and decreased FEV <sub>1</sub> in boys but not girls; parent-child correlations for FEV <sub>1</sub> for girls not boys	Lebowitz, 1984 [25]	adjusted for gender	none reported
none reported	Lebowitz et al., 1984 [63]	adjusted for gender	none reported
none reported	Lebowitz et al., 1987 [64]	gender	Vmax <sub>50%</sub> /FVC of females aged 13-25 > males of the same age; gender was a significant covariable in multivariate analysis of factors determining the relationship between symptoms, smoking and pulmonary function of children but not in relationship between asthma and pulmonary function (FEV <sub>1</sub> and Vmax <sub>50%</sub> )
male gender has positive influence on change in FEV <sub>1</sub> over a one year period	Lebowitz/Holberg, 1987 [65]	gender	none observed for FEV <sub>1</sub> , Vmax <sub>50%</sub> , and Vmax <sub>50%</sub> /FVC
decrement in FEV <sub>1</sub> associated with smoking in males > females	Tashkin et al., 1984 [26]	gender	FVC, FEV <sub>1</sub> , FEF <sub>25-75</sub> , Vmax of males > females; age-gender influences on the association between maternal smoking and pulmonary function (see Table 10)
none reported	Vedal et al., 1984 [66]	adjusted for gender	gender significant predictor of all pulmonary function parameters (FVC and FEV <sub>0.75</sub> boys > girls; FEF <sub>25-75</sub> , Vmax <sub>50%</sub> girls > boys); significant interaction between gender and age for all functional parameters except FVC; maternal smoking associated with decreased flow rates in girls, no association with maternal smoking in boys
none reported, no observed influence on maternal smoking association with pulmonary function			
unadjusted FEV <sub>1</sub> and FVC of boys > girls between 6-13 yrs of age			

*ETS Exposure, Confounding Variables and Respiratory Health in Children*

Published Study	Parameter (ages)	Association of Parameters
Spinaci et al., 1985 [31]	gender	gender influenced association between geographic area (outdoor pollution) and pulmonary function; no gender influences observed with regard to association between passive or active smoking and pulmonary function
Burchfiel et al., 1986 [32]	gender	age adjusted FEV <sub>1</sub> and FVC in males > females between 10-14 yrs of age; no consistent gender difference in Vmax <sub>25-75</sub> ; parental smoking decreased FEV <sub>1</sub> and FVC in males and Vmax <sub>25</sub> in females
Chen/Li, 1986 [67]	gender	paternal smoking was associated with greater decrements in FEV <sub>1</sub> , MMEF and FEF <sub>25-75</sub> in girls than boys
Murray/Morrison, 1986 [68]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender	NA (matched)
Teculescu et al., 1986 [37]	exposed and nonexposed subjects matched for gender	parental smoking associated with decreased FEV <sub>1</sub> and FEF <sub>25-75</sub> (not FVC or FEV <sub>1</sub> /FVC) in boys not girls
Evans et al., 1987 [69]	gender	none reported
Stern et al., 1987, 1989 [40, 41]	adjusted for gender	none reported
Tsimoyianis et al., 1987 [42]	gender	association between ETS exposure and abnormal FEF <sub>25-75</sub> or cough statistically significant in girls but not boys
Dijkstra et al., 1988 [44]	gender	NO <sub>2</sub> or gas stove usage was associated with decrements of pulmonary function growth in girls (FEV <sub>1</sub> and MMEF) not boys while household smoking was associated with decrements in pulmonary function growth in boys (PEF) not girls

*ETS Exposure, Confounding Variables and Respiratory Health in Children*

Published Study	Parameter
Martinez et al., 1988 [70]	gender
Masi et al., 1988 [71]	gender
Murray/Morrison, 1988 [72]	exposure maternal for maternal action
Chan et al., 1989 [73]	adjusted
Kauffmann et al., 1989 [74]	gender

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Association of Parameter(s)	Published Study	Parameter (ages)	Association of Parameter(s)
gender influenced association between geographic area (outdoor pollution) and pulmonary function; no gender influences observed with regard to association between passive or active smoking and pulmonary function	Martinez et al., 1988 [70]	gender	parental smoking associated with increased bronchial responsiveness (carbachol) in males not females; amount of parental smoking associated with skin test reactivity in males not females; interaction between gender, parental smoking and atopy confirmed by multivariate analysis.
age adjusted FEV <sub>1</sub> and FVC of males > females between 10-19 yrs of age; no consistent gender difference in Vmax <sub>50</sub> ; parental smoking decreased FEV <sub>1</sub> and FVC in males and Vmax <sub>50</sub> in females	Masi et al., 1988 [71]	gender	duration of ETS exposure at home (persons X years) associated with decreased FEV <sub>25-75</sub> and Vmax <sub>50</sub> (not FVC, FEV <sub>1</sub> , PEFR) in males not females; ETS exposure in men (not women) before 17 years if age associated with decreased FEV <sub>25-75</sub>
paternal smoking was associated with greater decrements in FEV <sub>1</sub> , MMEF, and FEF <sub>62.5-125</sub> in girls than boys	Murray/Morrison, 1988 [72]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender	NA (matched)
asth- NA (matched)	Chan et al., 1989 [73]	adjusted for gender	gender was a significant predictor of FVC, FEV <sub>0.75</sub> , MEF <sub>0.75</sub> , and PEFR; low birth weight was associated with a greater decrement of FEV <sub>0.75</sub> in boys than girls
parental smoking associated with decreased FEV <sub>1</sub> and FEF <sub>25-75</sub> (not FVC or FEV <sub>1</sub> /FVC) in boys not girls	Kauffmann et al., 1989 [74]	gender	FVC and FEV <sub>1</sub> boys > girls, no gender difference for FEF <sub>25-75</sub> , FEV <sub>1</sub> /FVC, or FEF <sub>25-75</sub> /FVC; differences noted in brother-brother and sister-sister correlations of specific pulmonary function parameters; for most pulmonary function parameter correlations, like-sex sibships > opposite-sex sibships; gender differences in pulmonary function growth patterns observed; gender differences in parent-child correlations of specific pulmonary function parameters observed.
none reported			
none reported			
association between ETS exposure and abnormal FEF <sub>25-75</sub> or cough statistically significant in girls but not boys			
NO <sub>2</sub> or gas stove usage was associated with decrements in pulmonary function growth in girls (FEV <sub>1</sub> and MMEF not boys) while household smoking was associated with decrements in pulmonary function growth in boys (PEF) not girls			

Published Study	Parameter (ages)	Association of Parameter
Murray/Morrison, 1989 [75]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender in some but not all analyses	maternal smoking associated with decreased FEV <sub>1</sub> , FEV <sub>0.75</sub> and PC <sub>20</sub> (not FVC) in girls
Strachan et al., 1990 [53]	adjusted for gender	none reported

Eleven pulmonary function endpoint studies suggested an interaction between gender of the subject and parental/household smoking [11, 56, 57, 62, 67, 37, 42, 44, 70, 75]. An interaction between gender, age and parental household smoking was suggested in two studies [26, 71], and that of atopy and parental/household smoking in one study [70]. Although a significant number of studies reported the involvement of gender in the association between parental/household smoking and pulmonary function, there was no consistency of this association with males versus females. Interactions between gender of the subject and other variables were also suggested, including age [66], smoking [59], smoking and symptoms [64], indoor pollution [61, 44], outdoor pollution [31], family history of asthma [11], low birth weight [73], parent-child pulmonary function correlations [57, 74], and sibling-sibling pulmonary function correlations [74]. Eleven studies provided no information concerning any association between gender and pulmonary function [15, 17, 39, 28, 21, 62, 25, 63, 69, 40, 41, 53].

#### F. Active smoking by the subject

As shown in Table 10, 20 clinical endpoint studies considered active smoking as a potential confounder. The criteria employed to evaluate this factor varied significantly from study to study. In some, the data on active smoking were obtained from parental responses, while in others they were based on childhood responses in the absence of parents. Several studies assumed children to be nonsmokers below a certain age, although the cut-off age selected by particular studies ranged from 12 to 16 years. There was also variation in the criteria employed (e.g. number of cigarettes smoked, etc.) to classify a child as a smoker. Smokers were excluded or considered by the authors to be insignificant in nine of these studies [8, 10, 19, 26, 28, 37, 38, 42, 44]. Three studies reported no observed association between active smoking and respiratory conditions in children [17, 23, 52]. Four studies reported that active smoking was associated with increased prevalence of respiratory symptoms and disease in children [13, 24, 31, 54] and none reported an opposite association. Four studies provided no information with regard to any association between smoking and clinical endpoints [11, 32, 39, 51].

Table 10. Consideration of Active Smoking in Household Smoking and Respiratory Health in Children

Published Study	Parameter
Cameron et al., 1969 [8]	2% of 13-14 year olds smoked, included in analysis
Lebowitz/Burrows, 1976 [10]	children assumed to be 2 of 60 14-15 year olds any smoked
Schilling et al., 1977 [11]	smoking from child
Bland et al., 1978 [13]	all children (grouped by cigarette consumption)
Weiss et al., 1980 [17]	childhood obtained responses from parents
Dodge, 1982 [19]	children reported
Schenker et al., 1983 [23]	whether more currently smoking
Charlton, 1984 [24]	quantitative smoking
Tashkin et al., 1984 [26]	children to be asked, and, if analyzed
Ware et al., 1984 [28]	children higher status (1st to 4th of smoking)
Spinaci et al., 1985 [31]	children one cigarette smoked

Association of Parameter(s)  
 Maternal smoking associated  
 with decreased FEV<sub>1</sub>, FEF<sub>25-75</sub>,  
 and PC<sub>20</sub> (not FVC) in boys not  
 girls  
 none reported

suggested an interaction  
 of smoking [11, 56, 57, 66,  
 gender, age and parental/  
 71], and that of atopy and  
 though a significant number  
 the association between  
 there was no consistency  
 tions between gender of  
 including age [66], smoking  
 [51, 44], outdoor pollution  
 [5], parent-child pulmonary  
 function correlations  
 concerning any association  
 [28, 21, 62, 25, 63, 69, 40].

considered active smoking  
 to evaluate this factor varied  
 as on active smoking were  
 they were based on childhood  
 studies assumed children to be  
 off age selected by particular  
 also variation in the criteria  
 to classify a child as a smoker  
 or to be insignificant in many  
 Three studies reported no  
 and respiratory conditions and  
 active smoking was associated  
 with disease in children [14,  
 15]. Four studies provided  
 between smoking and clinical

Table 10. Consideration of Active Smoking by the Subject in Studies of Parental/  
 Household Smoking and Respiratory Symptoms and Disease in Older  
 Children

Published Study	Parameter	Association of Parameter(s)
Cameron et al., 1969 [8]	2% of 13-16 yr olds reported smoking, apparently included in analysis	NA (homogeneous)
Lebowitz/Burrows, 1976 [10]	children under 15 were presumed to be nonsmokers (only 2 of 60 14 yr olds indicated any smoking and they had smoked very few cigarettes)	NA (homogeneous)
Schilling et al., 1977 [11]	smoking status obtained from child responses	none reported
Bland et al., 1978 [13]	all children questioned (grouped on basis of number cigarettes smoked)	associated with increased cough and breathlessness
Weiss et al., 1980 [17]	childhood smoking status obtained from subject's response in absence of parents	none observed for persistent wheeze
Dodge, 1982 [19]	children questioned, none reported smoking	NA (homogeneous)
Schenker et al., 1983 [23]	whether child smoked 5 or more cigarettes and is currently smoking (child's response)	none observed for respiratory symptoms (cough, phlegm, wheeze)
Charlton, 1984 [24]	quantity of cigarettes smoked/week (child response)	associated with increased cough
Tashkin et al., 1984 [26]	children under 12 assumed to be nonsmokers; others asked about smoking status and, if so, excluded from analysis	NA (homogeneous)
Ware et al., 1984 [28]	children in 4th grade or higher asked about smoking status in absence of parent (1st to 3rd grades from parental responses); incidence of smoking rare and; therefore not considered a risk factor	NA (homogeneous)
Spinaci et al., 1985 [31]	children who smoked at least one cigarette considered smokers (child's response)	associated with increased chronic cough

Published Study	Parameter (ages)	Association of Parameters
Burchfiel et al., 1986 [32]	Children under 16 yrs. considered to be nonsmokers (active smoking by older children determined by questionnaire)	none reported
Teculescu et al., 1986 [37]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Willat, 1986 [38]	none of the children smoked (based upon parental responses)	NA (homogeneous)
O'Connor et al., 1987 [39]	obtained from child's responses; adjusted for in analysis	none reported
Tsimoyianis et al., 1987 [42]	smokers or ex-smokers were excluded from study (based upon subject's responses)	NA (homogeneous)
Dijkstra et al., 1988 [44]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Charlton/Blair, 1989 [54]	sometimes or regular smoking compared to no smoking (child response)	associated with increased school absence for a variety respiratory and nonrespiratory ailments
Neuspeil et al., 1989 [51]	from parental interview	none reported
Sherman et al., 1990 [52]	smoking status obtained from child's responses	none observed for asthma

27 pulmonary function endpoint studies considered active smoking by the subject as a potential confounding variable (Table 11). As in the clinical endpoint studies, there was significant variation as to whether this information was provided by parent or child, the age below which children were assumed to be nonsmokers (9-16 years), and the amount a child needed to smoke to be classified as a smoker. Children were excluded on the basis of active smoking or were considered to be of insignificant number in 14 studies [28, 60, 19, 26, 66, 67, 68, 37, 69, 42, 44, 71, 72, 75]. Six studies reported that active smoking was associated with decreased pulmonary function [15, 58, 59, 64, 65, 31], none reported an opposite association, and two studies reported no observed association between active smoking and pulmonary function [57, 17]. In five pulmonary function endpoint studies, no information was provided on this issue [11, 39, 62, 63, 32].

Table 11. Consideration of Active Household Smoking and

Published Study	Parameter
Schilling et al., 1977 [11]	smoking child excluded
Tager et al., 1976 [57]	child's (detail although parent old or
Tager et al., 1979 [15]	child's (obtained response)
Weiss et al., 1980 [17]	child's obtained in absence
Tager et al., 1983 [58]	child's (obtained respiratory)
Tager et al., 1985 [59]	child's (obtained respiratory)
O'Connor et al., 1987 [39]	obtained from parent's analysis
Ware et al., 1984 [28]	child's high status (1st part of study: other risk)
Berkey et al., 1986 [60]	child's at lower (each grade smoking)
Dodge, 1982 [19]	child's reported
Lebowitz et al., 1982 [62]	active smoking



Association of Parameter(s)
none reported
NA (homogeneous)
NA (homogeneous)
none reported
NA (homogeneous)
NA (homogeneous)
associated with increased school absence for a variety of respiratory and nonrespiratory ailments
none reported
none observed for asthma

dered active smoking by the  
 1). As in the clinical endpoint  
 whether this information was  
 children were assumed to be  
 child needed to smoke to be  
 on the basis of active smoking  
 r in 14 studies [28, 60, 19, 20]  
 reported that active smoking  
 on [15, 58, 59, 64, 65, 31], none  
 studies reported no observed  
 nary function [57, 17]. In five  
 ation was provided on this issue

Table 11. Consideration of Active Smoking by the Subject in Studies of Parental/  
 Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameter(s)
Schilling et al., 1977 [11]	smoking status obtained from child responses; smokers excluded from analysis	none reported
Tager et al., 1976 [57]	childhood smoking history (details not specified although data obtained from parents for children 12 years old or less)	none observed for FEV <sub>1</sub> for males and females analyzed separately (stated that n was small)
Tager et al., 1979 [15]	child's smoking history (obtained from subject's responses)	associated with decreased FEF <sub>25-75</sub>
Weiss et al., 1980 [17]	childhood smoking status obtained from subject's response in absence of parents	none observed for FEF <sub>25-75</sub>
Tager et al., 1983 [58]	child's smoking history (obtained from subject's responses)	associated with decreased FEV <sub>1</sub> growth; effect on FEF <sub>25-75</sub> borderline (p=0.058)
Tager et al., 1985 [59]	child's smoking history (obtained from subject's responses)	associated with decreased FEV <sub>1</sub> and FEF <sub>25-75</sub>
O'Connor et al., 1987 [39]	obtained from child's responses; adjusted for in the analysis	none reported
Ware et al., 1984 [28]	children in 4th grade or higher asked about smoking status in absence of parent (1st to 3rd grades from parental responses; incidence of smoking rare and, therefore, not considered a risk factor)	NA (homogeneous)
Berkey et al., 1986 [60]	children who currently smoked at least 1 cigarette/week were excluded from study (each child in 4th or higher grades asked about personal smoking habits)	NA (homogeneous)
Dodge, 1982 [19]	children questioned, none reported smoking	NA (homogenous)
Lebowitz et al., 1982 [62]	active smoking (details not specified)	none reported

Published Study	Parameter	Association of Parameters
Lebowitz et al., 1984 [63]	based upon questionnaires completed by children 15 yrs and older	none reported
Lebowitz et al., 1987 [64]	current, ex-, or never smoker (obtained from children 15 yrs or older, otherwise from parent)	current and ex-smoking associated with decreased FEV <sub>1</sub> and Vmax <sub>25-75%</sub> levels and growth rates, and Vmax <sub>50%</sub> FEV <sub>1</sub>
Lebowitz/Holberg, 1987 [65]	childhood smoking (details not specified)	active smoking associated with decreased Vmax <sub>25-75%</sub> and Vmax <sub>50%</sub> /FVC, and FEV <sub>1</sub>
Tashkin et al., 1984 [26]	children under 12 assumed to be nonsmokers; others asked about smoking status and, if so, excluded from analysis	NA (homogeneous)
Vedal et al., 1984 [66]	children considered smoker they smoked 5 or more cigarettes and were currently smoking (obtained from subject's responses in grades 4-6, not 1-3); smokers excluded from study	NA (homogeneous)
Spinaci et al., 1985 [31]	children who smoked at least one cigarette was considered a smoker (child's response)	active smoking associated with decreased FEV <sub>25-75%</sub> and Vmax <sub>50%</sub>
Burchfiel et al., 1986 [32]	children under 16 yrs. considered to be nonsmokers (active smoking by older children determined by questionnaire)	none reported
Chen/Li, 1986 [67]	children who reported smoking 1 or more cigarettes/wk. were rare and were excluded from the study (based on subject's responses)	NA (homogeneous)
Murray/Morrison, 1986 [68]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)
Teculescu et al., 1986 [37]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Evans et al., 1987 [69]	ever smoking children were excluded from study (subject's responses)	NA (homogeneous)

Published Study
Tamoyianis et al., 1987 [42]
Dijkstra et al., 1988 [44]
Masi et al., 1988 [71]
Murray/Morrison, 1988 [72]
Murray/Morrison, 1989 [75]

#### G. Infant feeding

As shown in Table 12A, (i.e., presence or absence of milk) observed no association between lack of breast feeding provided no information or there were no pulmonary function data dealt with infant feeding.

Table 12. Consideration of Household Smoking Children

A. Infant feeding
Published Study
Fergusson/Horwood, 1985 [29]
Horwood et al., 1985 [30]
McConnochie/Roghmann, 1986 [33]
Willat, 1986 [38]

Association of Parameter(s)
none reported
current and ex-smoking associated with decreased FEV <sub>1</sub> and Vmax <sub>50</sub> levels and growth rates, and Vmax <sub>50</sub> /FVC
active smoking associated with decreased Vmax <sub>50</sub> and Vmax <sub>50</sub> /FVC, and FEV <sub>1</sub>
NA (homogeneous)
NA (homogeneous)
active smoking associated with decreased FEV <sub>1</sub> and Vmax <sub>50</sub>
none reported
NA (homogeneous)
NA (homogeneous)
NA (homogeneous)

Published Study	Parameter	Association of Parameter(s)
Tsimoyanis et al., 1987 [42]	smokers or ex-smokers were excluded from study (based upon subject's responses)	NA (homogeneous)
Dijkstra et al., 1988 [44]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Masi et al., 1988 [71]	all nonsmokers based upon subject's questionnaire responses	NA (homogeneous)
Murray/Morrison, 1988 [72]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)
Murray/Morrison, 1989 [75]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)

### G. Infant feeding

As shown in Table 12A, three of the six studies that addressed infant feeding (i.e., presence or absence of breast feeding or comparison of breast, formula or milk) observed no association [30, 38, 51], one paper reported an association between lack of breast feeding and increased wheezing [33], and two papers provided no information on this issue [29, 43]. As indicated in Tables 1 and 13A, there were no pulmonary function endpoint studies in school-age children that dealt with infant feeding.

Table 12. Consideration of Selected Potential Confounders in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

A. Infant feeding		
Published Study	Parameter	Association of Parameter(s)
Fergusson/Horwood, 1985 [29]	presence or absence of breast feeding	none reported
Horwood et al., 1985 [30]	early feeding history (breast and/or bottle) up to 4 mos. of age	none observed for asthma
McConnochie/Rogghmann, 1986 [33]	breast, formula, milk feeding during first 6 mos. of life	lack of breast feeding assoc. with incr. wheezing (strongest among children without family history of allergy)
Willat, 1986 [38]	method of postnatal feeding	none observed for sore throats

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*ETS Exposure, Confound*

Published Study	Parameter	Association of Parameters
Andrae et al., 1988 [43]	type of feeding during first 6 mos. of life	none reported
Neuspeil et al., 1989 [51]	breast feeding at least 1 month	none observed for wheeze, bronchitis
<b>B. Outdoor pollution</b>		
Published Study	Parameter	Association of Parameters
Kasuga et al., 1979 [14]	living distance from main highway as surrogate for amounts of NO <sub>2</sub> and SO <sub>2</sub> (<50 m, <100 m, >100 m); distance from highway based upon previous measurements of these gases	none observed for this parameter alone; however, increased prevalence rate of respiratory diseases in children of heavy smoking households living <50 m of highway, suggestive of interaction between outdoor pollution and ETS exposure
Tager et al., 1979 [15]	outdoor air quality reported to be similar in various parts of the community	NA <sup>1</sup> (homogeneous)
Speizer et al., 1980 [16]	NO <sub>2</sub> monitoring outdoors in selected households	none reported
Dodge, 1982 [19]	towns with copper smelters vs. towns without copper smelters	none observed for asthma, wheeze, and sputum; increased prevalence of cough associated with towns with copper smelters.
Schenker et al., 1983 [23]	regions of low, medium, and high air pollution (based upon mining and power plants)	none reported
Charlton, 1984 [24]	industrial vs. non-industrial regions	none observed for prevalence of cough
Lebowitz, 1984 [25]	"random cluster sample" for TSPs, RSPs, CO, O <sub>3</sub> , pollen, bacilli, fungi, and algae, over a 72 hr period	none reported
Ware et al., 1984 [28]	air quality variations among the 6 locations in this study were adjusted for by city-cohort correction in multiple logistic regression model	none reported

Published Study	Pa
Spinaci et al., 1985 [31]	ox by ar gr (l a
Teculescu et al., 1986 [37]	st a F
Stern et al., 1987, 1989 [40, 41]	a v c
Andrae et al., 1988 [43]	c F f
Angioni et al., 1989 [47]	i s
<b>C. Day care</b>	
Published Study	
Said et al., 1978 [12]	
Willat, 1986 [38]	
Andrae et al., 1988 [43]	
McConnochie/Rogghmann, 1989 [50]	
<b>D. Animal exposures</b>	
Published Study	
Fergusson/Horwood, 1985 [29]	
Horwood et al., 1985 [30]	
McConnochie/Rogghmann, 1986 [33]	
Andrae et al., 1988 [43]	

Association of Parameter(s)
none reported
none observed for wheezy bronchitis
Association of Parameter(s)
none observed for this parameter alone; however, increased prevalence rate of respiratory diseases in children of heavy smoking households living <50 m of highway suggestive of interaction between outdoor pollution and ETS exposure.
NA (homogeneous)
none reported
none observed for asthma, wheeze, and sputum; increased prevalence of cough associated with towns with copper smelters.
none reported
none observed for prevalence of cough
none reported
none reported

Published Study	Parameter	Association of Parameter(s)
Spinaci et al., 1985 [31]	outdoor pollution (monitored by daily measurement of SO <sub>2</sub> and TSPs) was basis of 3 geographic areas, central urban (UC), peripheral (UP), and suburban (SU).	bronchial secretions with colds increased (boys not girls) in UC and UP compared to SU; asthma increased (boys not girls) in SU compared to UC and UP; none observed for cough, wheeze, shortness of breath, infant or recent respiratory illness.
Teculescu et al., 1986 [37]	subjects recruited from an area without significant air pollution	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all towns examined were small with no significant sources of industrial air pollution	NA (homogeneous)
Andrae et al., 1988 [43]	compared area near pulp and paper plant to area farthest from plant	associated with increased bronchial hyperreactivity and allergic disease
Angioni et al., 1989 [47]	industries, workshops, joiners shops, bakeries near house	none observed for allergic respiratory and nonrespiratory disease
C. Day care		
Published Study	Parameter	Association of Parameter(s)
Said et al., 1978 [12]	day care before age of 3	day care associated with increased incidence of adenoidectomy and/or tonsillectomy
Willat, 1986 [38]	age starting at day care or nursery	none reported
Andrae et al., 1988 [43]	type of daily care for pre-schoolers	none reported
McConnochie/Rogghmann, 1989 [50]	"pre-school experience"	none observed for wheezing or asthma
D. Animal exposures		
Published Study	Parameter	Association of Parameter(s)
Fergusson/Horwood, 1985 [29]	duration of household pet ownership	none reported
Horwood et al., 1985 [30]	ownership of pet cat or dog	none observed
McConnochie/Rogghmann, 1986 [33]	pets in home	none observed
Andrae et al., 1988 [43]	caged birds, aquarium fish, and furred pets in home	none observed

Published Study	Parameter	Association of Parameters
Dijkstra et al., 1988 [44]	animals at home	none reported
Angioni et al., 1989 [47]	pets in house	none observed
Chan et al., 1989 [49]	pets in house	none reported
McConnochie/Rogghmann, 1989 [50]	dog or cat present in home	none observed
<b>E. Stress</b>		
Published Study	Parameter	Association of Parameters
Fergusson/Horwood, 1985 [29]	quantitative score for stressful events in mother's life	none reported
Horwood et al., 1985 [30]	quantitative scores for stressful events in mother's life and maternal depression	none observed
Neuspeil et al., 1989 [51]	quantitative score of maternal depression	none reported
!Not applicable		

Table 13. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Pulmonary Function in Older Children

<b>A. Infant feeding - no studies</b>		
<b>B. Outdoor pollution</b>		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	outdoor air quality reported to be similar in various parts of the community	NA (homogeneous)
Speizer et al., 1980 [16]	NO <sub>2</sub> monitoring outdoors in selected households	none reported
Ware et al., 1984 [28]	air quality variations among the 6 locations in this study were adjusted for by city-cohort correction in multiple logistic correction model	none reported
Hasselblad et al., 1981 [61]	ambient air pollution measurement of TSPs, RSPs, and water soluble sulfate fraction of TSPs	none observed for FEV <sub>0.75</sub>
Dodge, 1982 [19]	towns with copper smelters vs. towns without copper smelters	none observed for FEV <sub>1</sub>

Published Study	Parameter
Lebowitz et al., 1982 [62]	measure outdoor household low; par and NC in exce
Lebowitz, 1984 [25]	random TSPs, P bacilli, over a
Tashkin et al., 1984 [26]	adjust area
Spinaci et al., 1985 [31]	outdoor by da and T graph (UC) subur
Chen/Li, 1986 [67]	outdoor cons: subje samp
Teculescu et al., 1986 [37]	subje with
Stern et al., 1987, 1989 [40, 41]	all to with of ir
Kauffmann et al., 1989 [74]	town
<b>C. Day care - no studies</b>	

Association of Parameter(s)
none reported
none observed
none reported
none observed
Association of Parameter(s)
none reported
none observed
none reported

finders in Studies of Parental  
Action in Older Children

Association of Parameter(s)
NA (homogeneous)
none reported
none reported
none observed for FEV <sub>1</sub>
none observed for FEV <sub>1</sub>

Published Study	Parameter	Association of Parameter(s)
Lebowitz et al., 1982 [62]	measurement of a variety of outdoor pollutants in selected households (CO was considered low; particulates considered high; and NO <sub>2</sub> was variable but not in excess of NAAQS)	NA (homogeneous)
Lebowitz, 1984 [25]	"random cluster sample" for TSPs, RSPs, CO, O <sub>3</sub> , pollen, bacilli, fungi, and algae over a 72 hr period	children's Vmax inversely associated with TSPs and O <sub>3</sub> as an interaction; O <sub>3</sub> associated with Vmax in children not exposed to ETS.
Tashkin et al., 1984 [26]	adjustment for geographical area	none reported
Spinaci et al., 1985 [31]	outdoor pollution (monitored by daily measurement of SO <sub>2</sub> and TSPs) was basis of 3 geographic areas: central urban (UC), peripheral (LP), and suburban (SU).	UC and LP associated with decreased FEV <sub>1</sub> and FVC
Chen/Li, 1986 [67]	outdoor urban air pollution considered the same for all subjects because area of sample collection small	NA (homogeneous)
Teculescu et al., 1986 [37]	subjects recruited from an area without significant air pollution	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all towns examined were small with no significant sources of industrial pollution	NA (homogeneous)
Kauffmann et al., 1989 [74]	town of residence	none reported
C. Day care - no studies		

D. Animal exposures		
Published Study	Parameter	Association of Parameters
Murray/Morrison, 1986 [68]	matched for ownership of household pets	NA (matched)
Murray/Morrison, 1988 [72]	matched for ownership of furred household pets	none observed when tested by multiple regression on a seasonal basis
Chan et al., 1989 [73]	pets in house	none reported
Murray/Morrison, 1989 [75]	matched for ownership of dogs or cats and positive skin prick tests to appropriate species	NA (matched)
E. Stress		
Published Study	Parameter	Association of Parameter(s)
Evans et al., 1987 [69]	general stress in household	none reported

#### H. Outdoor pollution

As shown in Table 12B, the 13 clinical endpoint papers that considered outdoor pollution employed a variety of criteria for this particular potential confounder, including proximity to an area of pollution (e.g., highway or industrial source), residence within an industrial area, and measured levels of industrial pollution using specific environmental markers. Four of the studies reported no observed association [14, 24, 31, 47] and three reported positive associations between outdoor pollution and particular clinical endpoints [19, 31, 43]. One study suggested an interaction between outdoor pollution and parental household smoking [14]. In three of these studies, the outdoor air quality of the area(s) was judged to be similar or homogeneous by the authors [15, 37, 40, 41], while four papers provided no information pertaining to associations [16, 23, 25, 28].

As shown in Table 13B, outdoor pollution (i.e., on the basis of proximity to industrial areas or environmental markers) was considered in 13 of these studies. Outdoor air quality was regarded as being homogeneous in five studies [15, 62, 67, 37, 40, 41]. No association with outdoor pollution was reported to be observed in two studies [61, 19], while a "negative" association between particular pulmonary function parameters and outdoor pollution was reported in two studies [25, 31]. Four studies reported no information on any association between outdoor pollution and pulmonary function endpoints [16, 28, 26, 74].

#### I. Day care

Of the four clinical endpoint studies that dealt with day care use as a potential confounder, one reported no observed association [50], one reported a "positive" association [12], and two provided no information relative to any association [38,

43] (Table 12 C). As indicated in Table 12 C, as indicated in the function endpoint studies c

#### J. Animal exposures

Five of the eight studies (cared furred pets) reported [33, 43, 47, 50] while the information (Table 12 D). Furred pets as a potential confounder in these studies. Of these, two were observed association [72], (Table 13 D).

#### H. Stress

The three clinical endpoint studies employed a questionnaire as a confounding variable and two provided no information on general stress in the household (Table 13 E).

#### I. Dampness and cold

As shown in Table 14 A, dampness and cold as a potential confounder in the clinical endpoint studies on outdoor humidity; indoor and/or dampness in the household. Dampness and cold were observed in two of the clinical endpoint studies. Dampness and cold in the household increased rates of respiratory infections. The clinical endpoint studies provided no information on the association with clinical endpoints [16, 28, 26, 74].

Of the four pulmonary function studies, two reported an association between dampness and cold (e.g., outdoor air quality and cold/wet season vs. indoor air quality) but no association between dampness and cold and maternal smoking and day care use [44, 73] (Table 15 A).



	Association of Parameter(s)
	NA (matched)
	none observed when tested by multiple regression on a seasonal basis
	none reported
	NA (matched)
	Association of Parameter(s)
	none reported

point papers that considered a for this particular potential pollution (e.g., highway or and measured levels of ers. Four of the studies and three reported positive particular clinical endpoints [19, 31, outdoor pollution and parental as, the outdoor air quality of the s by the authors [15, 37, 40, 41]. ning to associations [16, 23, 25].

... on the basis of proximity to considered in 13 of these studies. homogeneous in five studies [15, 62] - pollution was reported to be "negative" association between outdoor pollution was reported information on any association action endpoints [16, 28, 26, 74].

... with day care use as a potential son [50], one reported a "positive" on relative to any association.

43] (Table 12 C). As indicated in Tables 1 and 13C, none of the pulmonary function endpoint studies dealt with day care.

#### J. Animal exposures

Five of the eight studies that dealt with animal exposures (mainly domesticated furred pets) reported no observed association with a clinical endpoint [30, 33, 43, 47, 50] while the remaining three [29, 44, 49] provided no relevant information (Table 12 D). Four studies considered animal exposures (household pets) as a potential confounding variable in pulmonary function endpoints studies. Of these, two were considered to be matched [68, 75], one reported no observed association [72], and one provided no information on the issue [73] (Table 13 D).

#### H. Stress

The three clinical endpoint papers that considered stress as a potential confounder employed a quantitative score of maternal stress and/or depression as a confounding variable. One of these reported no observed association [30] and two provided no information on this issue [29, 51] (Table 12 E). Stress (i.e., general stress in the household) was considered in one pulmonary function endpoint study [69] in which no information on associations was provided (Table 13 E).

#### I. Dampness and cold

As shown in Table 14 A, seven clinical endpoint studies considered dampness and cold as a potential confounder based upon the following types of criteria: outdoor humidity; indoor humidity; domestic dampness and mold; and coldness and/or dampness in the child's bedroom or home. No association was reported observed in two of the studies [47, 49], while three studies, all involving dampness and cold in the child's bedroom or home, reported associations with increased rates of respiratory symptoms and disease in subjects [36, 43, 50]. Two studies provided no information concerning dampness and cold and associations with clinical endpoints [25, 44].

Of the four pulmonary function endpoint studies that considered dampness and cold (e.g., outdoor and indoor humidity, dampness and/or cold in the home and cold/wet season vs. warm/dry season), one reported no observed independent association but an association suggestive of an interaction between season, maternal smoking and asthma [72], while three provided no such information [25, 44, 73] (Table 15 A).

Table 14. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Respiratory Symptoms and Disease in Older Children

A. Dampness and cold		
Published Study	Parameter	Association of Parameter(s)
Lebowitz, 1984 [25] Strachan/Elton, 1986 [36]	outdoor and indoor humidity dampness/mold in home; bedroom environment (cold)	none reported dampness/mold associated with increased rates of wheezing, school absences due to lower respiratory problems, and coughing; bedroom environment associated with increased wheezing.
Andrae et al., 1988 [43]	signs of damage due to dampness in home	associated with increased coughing after respiratory infections (not asthma, allergic rhinitis, or exercise-induced cough).
Dijkstra et al., 1988 [44]	dampness in the house	none reported
Angioni et al., 1989 [47]	absence of heating in home	none observed
Chan et al., 1989 [49]	dampness or cold in home	none observed
Neuspeil et al., 1989 [50]	dampness in child's bedroom	associated with increased wheezy bronchitis
B. Heating and air conditioning		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	homes with central gas heating vs. other	none reported
Speizer et al., 1980 [16]	home heating fuel (oil, gas, electric); presence or absence of air conditioning	none observed
Weiss et al., 1980 [17]	gas heater in kitchen heating	none observed
Ware et al., 1984 [28]	fuel and air conditioning (dropped from regression)	none reported
Spinaci et al., 1985 [31]	presence or absence of central heating	none reported
McConnochie/Rohgmann, 1986 [33]	home heating method	none observed
Strachan/Elton, 1986 [36]	type of heat (gas or coal)	coal burning associated with increased coughing
Andrae et al., 1988 [43]	type of heating	none reported
Angioni et al., 1989 [47]	type of heating (radiators, electric, gas, firewood, none)	none observed

Published Study	Parameter
Berwick et al., 1989 [48]	type of heat from tax
Chan et al., 1989 [49]	type of fuel heating
McConnochie/Rohgmann, 1989 [50]	home heating

C. Season	
Published Study	Parameter
Colley et al., 1974 [9]	cough in study
Bland et al., 1978 [13]	study correlation
Charlton, 1984 [24]	questionnaire of December variation epidemic
Lebowitz, 1984 [25]	season
Park/Kim, 1986, 1988 [34, 35]	season
Strachan/Elton, 1986 [36]	conductance season
Tsimoyianis et al., 1987 [42]	conductance
Dijkstra et al., 1988 [44]	questionnaire symptom

## D. Occupational exposures - no studies

E. Quality of housing	
Published Study	Parameter
Kasuga et al., 1979 [14]	structure reinforcement
Park/Kim, 1986, 1988 [34, 35]	number in a house
Strachan/Elton, 1986 [36]	145 of 1 in local
Andrae et al., 1988 [43]	type of building, carpeting
Berwick et al., 1989 [48]	from tax (assessment used, number of floors, bottom
Chan et al., 1989 [49]	home condition

finders in Studies of Parental/  
ptoms and Disease in Older

Association of Parameter(s)
none reported
dampness/mold associated with increased rates of wheezing, school absences due to lower respiratory problems, and coughing; bedroom environment associated with increased wheezing.
associated with increased coughing after respiratory infections (not asthma, allergic rhinitis, or exercise-induced cough).
none reported
none observed
none observed
associated with increased wheezy bronchitis
Association of Parameter(s)
none reported
none observed
none observed
none reported
none reported
none observed
coal burning associated with increased coughing
none reported
none observed

Published Study	Parameter	Association of Parameter(s)
Berwick et al., 1989 [48]	type of heating and fuel used from tax assessor's records	none reported
Chan et al., 1989 [49]	type of fuel used for home heating	none reported
McConnochie/Rogghmann 1989 [50]	home heating method	none observed
<b>C. Season</b>		
Published Study	Parameter	Association of Parameter(s)
Colley et al., 1974 [9]	cough in winter as endpoint	NA (homogeneous)
Bland et al., 1978 [13]	study conducted in July	NA (homogeneous)
Charlton, 1984 [24]	questionnaires were administered during the first week of December to minimize variations due to local season epidemics	NA (homogeneous)
Lebowitz, 1984 [25]	season	none reported
Park/Kim, 1986, 1988 [34, 35]	season	none observed
Strachan/Elton, 1986 [36]	conducted during winter season	NA (homogeneous)
Tsimoyianis et al., 1987 [42]	conducted during August	NA (homogeneous)
Dijkstra et al., 1988 [44]	questions on respiratory symptoms gathered in winter	NA (homogeneous)
<b>D. Occupational exposures - no studies</b>		
<b>E. Quality of housing</b>		
Published Study	Parameter	Association of Parameter(s)
Kasuga et al., 1979 [14]	structure of house (wood vs. reinforced concrete)	none observed
Park/Kim 1986, 1988 [34, 35]	number of rooms occupied in a house	none observed
Strachan/Elton, 1986 [36]	145 of 165 children lived in local authority housing	NA (homogeneous)
Andrae et al., 1988 [43]	type of house (construction, building material, wall to wall carpeting)	none observed
Berwick et al., 1989 [48]	from tax assessor records (assessed value, materials used, condition of home, age, number of rooms, number of floors, square footage of bottom floor)	none observed
Chan et al., 1989 [49]	home condition	none reported

**J. Heating and air conditioning**

Among the 12 clinical endpoint studies that considered heating and air conditioning, several criteria were employed, such as type of home heating fuel, presence or absence of air conditioning, and presence or absence of home heating (Table 14 B). Of these, five studies reported no observed association of this variable (usually pertaining to home heating) with clinical endpoints [16, 17, 33, 47, 50], while one study reported an association between coughing and the use of coal burning [36]. Six of these studies provided no information relative to any association with this particular potential confounding variable [15, 28, 31, 43, 48, 49].

Heating and air conditioning (i.e., type of home heating fuel, presence or absence of air conditioning, or presence or absence of central heating) were considered in nine pulmonary function endpoint studies (Table 15 B). Of these, one was considered to be homogeneous with regard to this potential confounder [62], three reported no observed association [16, 70, 72], and two reported that the type of home heating influenced pulmonary function [16, 31]. Four studies provided no information on the relationship between this potential confounder and pulmonary function [15, 28, 73, 75].

Table 15. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Pulmonary Function in Older Children

A. Dampness and cold		
Published Study	Parameter	Association of Parameter(s)
Lebowitz, 1984 [25]	outdoor and indoor humidity	none reported
Dijkstra et al., 1988 [44]	dampness in the house	none reported
Murray/Morrison, 1988 [72]	cold/wet season vs. warm/dry season	none observed for FEV <sub>1</sub> , FEF <sub>25-75</sub> , and PC <sub>20</sub> to histamine in asthmatic children of nonsmoking mothers although decrements of above observed in asthmatic children of smoking mothers compared to children of non-smoking mothers during cold/wet season.
Chan et al., 1989 [73]	dampness or cold in home	none reported
B. Heating and air conditioning		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	homes with central gas heating vs. other	none reported

Published Study	Parameter
Speizer et al., 1980 [16]	home heating fuel, electric or gas, type of air conditioning
Ware et al., 1984 [28]	heating from fireplace, electric, or gas
Lebowitz et al., 1982 [62]	most common type of heat source
Spinaci et al., 1985 [31]	presence of central heating
Martinez et al., 1988 [70]	source of heat (central gas, electric, or oil)
Murray/Morrison, 1988 [72]	type of heating system
Chan et al., 1989 [73]	type of heating system
Murray/Morrison, 1989 [75]	use of heating system

**C. Season**

Published Study	Parameter
Yarnell/St. Leger, 1979 [56]	all parameters of pulmonary function
Ware et al., 1984 [28]	seasonal variation in pulmonary function
Hasselblad et al., 1981 [61]	seasonal variation in pulmonary function
Lebowitz, 1984 [25]	seasonal variation in pulmonary function
Spinaci et al., 1985 [31]	seasonal variation in pulmonary function
Chen/Li, 1986 [67]	seasonal variation in pulmonary function
Tsimoyianis et al., 1987 [42]	seasonal variation in pulmonary function
Dijkstra et al., 1988 [44]	seasonal variation in pulmonary function
Martinez et al., 1988 [70]	seasonal variation in pulmonary function

considered heating and air type of home heating fuel, presence or absence of home no observed association of a clinical endpoints [16, 17, between coughing and the information relative to any variable [15, 28, 31, 43, 48, 49].

heating fuel, presence or absence of central heating) were listed (Table 15 B). Of these, no this potential confounder [72], and two reported that association [16, 31]. Four studies on this potential confounder

findings in Studies of Parental Smoking in Older Children

Association of Parameter(s)
none reported
none reported
none observed for FEV <sub>1</sub> , FEF <sub>25-75</sub> , and PC <sub>20</sub> to histamine in asthmatic children of nonsmoking mothers although decrements of above observed in asthmatic children of smoking mothers compared to children of nonsmoking mothers during cold/wet season.
none reported
Association of Parameter(s)
none reported

Published Study	Parameter	Association of Parameter(s)
Speizer et al., 1980 [16]	home heating fuel (oil, gas, electric); presence or absence of air conditioning	FEV <sub>1</sub> residuals vary as follows for home heating fuel: oil > gas > electric; none observed for presence or absence of air conditioning
Ware et al., 1984 [28]	heating fuel and air (dropped from regression)	none reported
Lebowitz et al., 1982 [62]	most homes had central heat and air conditioning	NA (homogeneous)
Spinaci et al., 1985 [31]	presence or absence of central heating	central heating associated with increased FVC
Martinez et al., 1988 [70]	source of energy for heating (centralized, kerosene, natural gas, other)	none observed for bronchial responsiveness
Murray/Morrison, 1988 [72]	type of central heating and use of wood stoves for heating	none observed for various types of home heating
Chan et al., 1989 [73]	type of fuel used for home heating	none reported
Murray/Morrison, 1989 [75]	use of wood stove for heating	none reported
<b>C. Season</b>		
Published Study	Parameter	Association of Parameter(s)
Yamell/St. Leger, 1979 [56]	all pulmonary function performed during summer months	NA (homogeneous)
Ware et al., 1984 [28]	seasonal adjustment for pulmonary function	none reported
Hasselblad et al., 1981 [61]	seasonal adjustment for pulmonary function	none reported
Lebowitz, 1984 [25]	seasonal adjustment for peak flow	none reported
Spinaci et al., 1985 [31]	study conducted during winter season (October to April)	NA (homogeneous)
Chen/Li, 1986 [67]	study conducted in June	NA (homogeneous)
Tsimoyianis et al., 1987 [42]	study conducted in August	NA (homogeneous)
Dijkstra et al., 1988 [44]	pulmonary function measured in spring and autumn	NA (homogeneous)
Martinez et al., 1988 [70]	pulmonary function measured during September and November	NA (homogeneous)

Published Study	Parameter	Association of Parameter(s)
Murray/Morrison, 1988 [72]	cold, wet season (October through May) vs. warm, dry season (June through September)	none observed for FEV <sub>1</sub> , FEF <sub>25-75</sub> , and PC <sub>20</sub> to histamine in asthmatic children of nonsmoking mothers, although decrements of above were observed in asthmatic children of smoking mothers compared to children of nonsmoking mothers during the cold, wet season
<b>D. Occupational exposures</b>		
Published Study	Parameter	Association of Parameter(s)
Kauffmann et al., 1989 [74]	parents were chosen from white collar workers to decrease any possible influence of parental exposure to industrial pollutants	NA (homogeneous)
<b>E. Quality of housing</b>		
Published Study	Parameter	Association of Parameter(s)
Lebowitz et al., 1982 [62]	housing quality said to be relatively uniform	NA (homogeneous)
Chan et al., 1989 [73]	home condition	none reported

### K. Seasons

As shown in Table 14 C, eight clinical endpoint studies considered season (i.e., time of year when questionnaire was administered or when endpoint was to have occurred). Of these studies, six were considered homogeneous with regard to season [9, 13, 24, 36, 42, 44], while one study reported no observed association [34, 35] and one study provided no information on this variable [25].

As shown in Table 15 C, the criteria for consideration of season pertained to when pulmonary measurements were taken. Of the 10 relevant studies, six were considered to be homogeneous [56, 31, 67, 42, 44, 70], one reported no independent association but a possible interaction of asthma, maternal smoking and season [72], while the remaining three studies provided no relevant data [28, 61, 25].

### L. Occupational exposures

No clinical endpoint studies dealt with occupational exposures of the parent or child as a potential confounding variable (Table 1 and Table 14 D). As shown in Table 15 D, one study [74] employed only white collar worker families to minimize occupational exposures of the subjects and was, thus, judged to be homogenous with regard to occupational exposures.

### M. Quality of housing

Several criteria were varied in the studies that considered quality of housing: basic structure of the home, home age, home home and particular aspects of home environment assessed value (Table 14 E). The association with a clinical endpoint was not homogeneous [36] and not homogeneous [36] and not homogeneous [36].

Housing quality was considered in only one endpoint studies, with one study provided no information on it.

Our recent analysis of 16 studies revealed that several factors between household/parental characteristics and diseases and pulmonary outcomes or older children [7]. Firstly, tobacco use, wheeze, asthma, or bronchitis in parents or adult household members, or medical records in only one of the 21 potential confounders was a question. For example, only one study with regard to the parent's education that they were considered (1/21).

In our previous report, we considered 16 variables (i.e., socioeconomic status, family health history, personal health history, and socioeconomic status, family health history).

The current report extends the analysis to the remaining 16 confounders. The analysis reveals wide variation in the association between housing quality and respiratory health.

association of Parameter(s)
ne observed for FEV <sub>1</sub> , F <sub>25-75</sub> , and PC <sub>20</sub> to asthma in asthmatic children of nonsmoking mothers, although decrements above were observed in asthmatic children of smoking mothers compared to children of nonsmoking mothers during the cold, wet season.
association of Parameter(s)
A (homogeneous)
association of Parameter(s)
A (homogeneous)
association of Parameter(s)
A (homogeneous)
association of Parameter(s)
A (homogeneous)

### M. Quality of housing

Several criteria were variably used in the six clinical endpoint studies that considered quality of housing as a potential confounding variable. Among these were basic structure of the home (wood vs. concrete), number of rooms in the home and particular aspects of the home, such as condition, square footage or assessed value (Table 14 E). Of these six studies, four reported no observed association with a clinical endpoint [14, 34, 35, 43, 48], while one was judged to be homogeneous [36] and one provided no relevant information [49].

Housing quality was considered as a variable in two pulmonary function endpoint studies, with one judged to be homogeneous [62] while the other provided no information on this issue [73] (Table 15 E).

## DISCUSSION

Our recent analysis of the treatment of potential confounding variables revealed that several factors could explain the lack of consistent association between household/parental smoking and the prevalence of respiratory symptoms and diseases and pulmonary function endpoints in studies of school age or older children [7]. Firstly, the clinical endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) were based largely on subjective responses of parents or adult household members and were verified by physical examination or medical records in only eight of the 45 studies. Secondly, relatively few of the 21 potential confounders identified were considered in the studies in question. For example, only eight of the 21 potential confounders (socioeconomic status, age, gender, gas stove usage, personal health history, family size, location of residence, and active smoking by subject) were considered in the majority of the clinical and/or pulmonary function endpoint epidemiologic studies, while several of the confounders (infant feeding, day care use, dampness/cold, occupational exposures, quality of housing, nutritional status) received little or no attention. In addition, most studies considered relatively few of the potential confounders and there was considerable variation from study to study with regard to the particular confounders considered, as well as the way that they were considered (i.e., statistical testing).

In our previous report, detailed analysis of selected potential confounding variables (i.e., socioeconomic status, gas stove usage, indoor pollution, family health history, personal health history) revealed significant variation from study to study in the criteria used for each variable, particularly in the case of socioeconomic status, family health history, and personal health history [7].

The current report extends these initial observations by examining in detail the remaining 16 confounding variables from the list of 21 such factors. This analysis reveals wide variation in the criteria used for several particular

studies considered season  
d or when endpoint was  
ered homogeneous with  
ly reported no observed  
tion on this variable [25]

on of season pertained to  
relevant studies, six were  
t, 70], one reported no  
sthma, maternal smoking  
no relevant data [26, 61, 25]

al exposures of the parent  
id Table 14 D). As shown  
collar worker families  
was, thus, judged to be

confounders, most notably family size, location of residence, age of the subject, active smoking, outdoor pollution, dampness and cold, type of heating and conditioning, and quality of housing.

Since confounders alone or in combination could potentially influence the outcome of epidemiologic studies, despite their consideration and/or adjustment in such studies [6], examination of the consistency of association between such factors and endpoints would seem to be an important endeavor. An indication of whether or not there was a consistent association from study to study relative to a particular confounder can be obtained by consideration of only those studies that addressed such an association (i.e., after exclusion of studies where confounders were judged by the authors to be matched, homogenous, or where associations were not reported). A consistency of association or lack of association is based upon whether the majority of studies favor an increase, decrease, or no association between the variable in question and the endpoint. These data for both the previous and current analysis are summarized for clinical and pulmonary function endpoints in Tables 16 and 17, respectively.

Our previous analysis revealed that family health history and personal health history were consistently associated with an increased prevalence of respiratory symptoms and disease (Table 16), while personal health history was consistently associated with decreased pulmonary function (Table 17) in index children. No association was consistently observed between clinical endpoints and gas stove usage/indoor pollution (Table 16) or between pulmonary function endpoints and socioeconomic status or family health history (Table 17). The results were equivocal (no consistent trend) with regard to socioeconomic status and clinical endpoints (Table 16), as well as gas stove/indoor pollution and pulmonary function endpoints (Table 17) [7].

The current report extends these observations. The majority of studies pertaining to gender indicate that males are more at risk for respiratory symptoms and diseases (Table 16). Among the factors found to consistently influence pulmonary function in index children were gender, age, active smoking and location of residence (Table 17). No association was consistently observed for clinical endpoints and family size, heating/air conditioning, animal exposures, quality of housing, and infant feeding (Table 16) and for pulmonary function endpoints and family size (Table 17). Caution should be exercised with regard to interpretation of a consistent lack of association between a potential confounder and an endpoint. Although such consistency may indicate that such confounders have little influence on the outcome of the study, this lack of association could also be a reflection of the wide variation from study to study in the criteria used for such variables, the fact that clinical endpoints were, for the most part unverified, and, in some cases, the relatively small number of studies involved.

Table 16. Associations Between Endpoints

<p><u><b>Increased/Decreased Prevalence of</b></u></p> <p>Family health history (increased)</p> <p>Personal health history (increased)</p> <p>Gender (males increased, 13 studies)</p>
<p><u><b>No Association Observed</b></u></p> <p>Gas stove use/indoor pollution</p> <p>Family size (10 of 13 studies)</p> <p>Heating/air conditioning (5 of 5 studies)</p> <p>Animal exposures (5 of 5 studies)</p> <p>Quality of housing (3 of 4 studies)</p> <p>Infant feeding (3 of 4 studies)</p>
<p><u><b>Equivocal/Uncertain Association:</b></u></p> <p>Socioeconomic status (20 studies)</p> <p>Location of residence (8 studies)</p> <p>Age (17 studies)</p> <p>Active smoking (7 studies)</p> <p>Outdoor pollution (6 studies)</p> <p>Dampness and cold (5 studies)</p> <p>Day care use (2 studies)</p> <p>Season (1 study)</p> <p>Stress (1 study)</p> <p>Occupational exposures (0 studies)</p> <p>Nutrition (0 studies)</p>

\*Number of studies after exclusion of studies with no association

In the current analysis there was no significant difference with regard to location of dampness/cold, day care, sex, or pulmonary function endpoint. Animal exposures, dampness/cold, could be due either to variation in animal exposures or to differences of studies involved. Also, as in the case of the other studies, the study could reflect lack of control or use of unverified subject

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Table 16. Associations Between Potential Confounding Variables and Clinical Endpoints

<u>Increased/Decreased Prevalence of Symptoms/Diseases</u>	
Family health history (increased, 16 of 17 studies*)	
Personal health history (increased, 11 of 11 studies)	
Gender (males increased, 13 of 23 studies)	
<u>No Association Observed</u>	
Gas stove use/indoor pollution (13 of 15 studies)	
Family size (10 of 13 studies)	
Heating/air conditioning (5 of 6 studies)	
Animal exposures (5 of 5 studies)	
Quality of housing (3 of 4 studies)	
Infant feeding (3 of 4 studies)	
<u>Equivocal/Uncertain Association or No Data Available</u>	
Socioeconomic status (20 studies)	
Location of residence (8 studies)	
Age (17 studies)	
Active smoking (7 studies)	
Outdoor pollution (6 studies)	
Dampness and cold (5 studies)	
Day care use (2 studies)	
Season (1 study)	
Stress (1 study)	
Occupational exposures (0 studies)	
Nutrition (0 studies)	
*Number of studies after exclusion of those matched; homogenous, and not reported.	

ence, age of the subject, old, type of heating/air

potentially influence the ration and/or adjustment association between such endeavor. An indication from study to study relative ation of only those studies usion of studies where d, homogenous, or where f association or lack of studies favor an increase, uestion and the endpoint. re summarized for clinical 17, respectively.

istory and personal health prevalence of respiratory th history was consistently 17) in index children. No al endpoints and gas stove onary function endpoints ah 17). The results were c status and clinical pollution and pulmonary

The majority of studies sk for respiratory symptoms d to consistently influence r, age, active smoking and s consistently observed for itioning, animal exposures. nd for pulmonary function ld be exercised with regard ation between a potential ency may indicate that such e of the study, this lack of ariation from study to study clinical endpoints were for relatively small number of

In the current analysis the associations are equivocal for clinical endpoints with regard to location of residence, active smoking, outdoor pollution, dampness/cold, day care, season, stress, and age of subject (Table 16) and for pulmonary function endpoints and heating/air conditioning, outdoor pollution, animal exposures, dampness/cold, and season (Table 17). Equivocal associations could be due either to variation of result from study to study, or the small number of studies involved. Also, as in the case of lack of association, variation from study to study could reflect lack of standardization of criteria for confounding variables or use of unverified subjective responses as clinical endpoints.

Table 17. Associations Between Potential Confounding Variables and Pulmonary Functional Endpoints

<b>Increased/Decreased Pulmonary Function</b>
Personal health history (decreased, 12 of 15 studies)
Age (increased, 11 of 12 studies)
Gender (males increased, 9 of 10 studies)
Active smoking (decreased, 6 of 8 studies)
Location of residence (decreased, 4 of 5 studies)
<b>No Association Observed</b>
Socioeconomic status (9 of 13 studies)
Family health history (7 of 8 studies)
Family size (7 of 7 studies)
<b>Equivocal/Uncertain Association or No Data Available</b>
Gas stove use/indoor pollution (11 studies)
Heating/air conditioning (4 studies)
Outdoor pollution (4 studies)
Animal exposures (1 study)
Dampness and cold (1 study)
Season (1 study)
Stress (0 studies)
Infant feeding (0 studies)
Nutrition (0 studies)
Quality of housing (0 studies)
Day care use (0 studies)
Occupational exposures (0 studies)
*Number of studies after exclusion of those matched, homogeneous, and not reported.

Taken together, the results of this analysis and the previous analyses of the published epidemiologic data in school-age children [1-3, 7] indicate lack of a consistent association between parental/household smoking and respiratory clinical and pulmonary function endpoints in these children, inconsistent and inadequate treatment of potential confounding variables and inadequate verification of clinical endpoints in studies based on parental responses to questionnaires. Until and unless these inconsistencies and inadequacies can be appropriately addressed and resolved, the available epidemiologic data do not justify a conclusion that there is even an association between parental or household smoking and adverse respiratory effects in children in this age group, let alone a relationship with ETS exposure.

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Confounding Variables and Pulmonary

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*ETS Exposure, Confounding Variables and Respiratory Health in Children*

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	AUT
AOYAGI, Mikiharu	237
BAEK, Sung-Ok	141
BITCOLOV, N.Z.	17
BROWN, Robert C.	185
BUCK, Manfred	13
CASTLEMAN, Barry I.	2
CHEN, Qigao	8
CHEN, Xinghua	12
CHEN, Yibin	20
DENG, Qiyuan	12
DU, Qingcheng	29
DUNG, Nguyen The	28
FUJIMURA, Mitsuru	26
HAHN, Myung-Ho	1-
HASHIMOTO, Yoshikazu	20
HE, Fengsheng	30
HE, F.	2
HISANAGA, Naomi	17
HÖEFERT, Norbert	2
HOLCOMB, Larry C.	
HOOD, Ronald D.	3
HOSKINS, John A.	1
HOU, Yuxi	2
HU, Gushua	2
HU, Xiu-Lan	1
HUANG, Jian	1
HUANG, Zhao-Hui	1

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## Indoor Air Quality in Asia

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## INDOOR AIR QUALITY IN ASIA

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## Review

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# Analysis of Potential Confounding Variables in Epidemiologic Studies of Parental/Household Smoking and Respiratory Health in Preschool Children

### Key Words

Respiratory illness in children  
Respiratory health in children  
Environmental tobacco smoke  
Parental smoking  
Respiratory infection  
Epidemiology  
Confounding variables  
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### Abstract

In this analytical study, aspects of the design of 41 epidemiologic studies pertaining to the relationship between parental/household smoking and the prevalence of respiratory symptoms and certain illnesses in preschool children (0-5 years old) were examined using a systematic protocol developed previously for a similar analysis of epidemiologic studies in school-age or older children. Wide variability was observed from study to study in the consideration of 21 predetermined potential confounding variables. While the socioeconomic status (SES), family health history, subject's personal health history, family size, age and gender were considered in 50% or more of the studies, indoor pollution (other than gas stove usage), day care use, animal exposures, stress, dampness/cold, season, occupational exposures, nutritional status of the subject, and maternal smoking during pregnancy were considered infrequently (in <25% of the studies) or not at all. A wide variation was also observed from study to study in the array of confounders considered. When evaluated on the basis of number of confounders considered per study, only 3 of the 41 papers considered 10 or more of the 21 predetermined variables. The clinical endpoints, usually obtained from parental questionnaire responses, were validated by medical records or physician examination in only slightly more than 50% (21/41) of the relevant epidemiologic studies. Twelve of the 21 predetermined confounders were analyzed in detail. There was wide variation in and a lack of standardization of the criteria used as indices of SES, family and personal health history, and age. There was also marked variation among the studies in methods used, if any, to adjust for confounding variables. Several of the confounding variables that we looked at appeared to be consistently associated with increased risk of respiratory illness in preschool children, including family and personal health history, young age, male gender, day care use and season. On the other hand, no consistent association was observed for SES, artificial feeding, gas fuel use and indoor pollution, while equivocal or uncertain data in this regard were obtained for dampness/cold and heating/air-conditioning. While no consistent interactions between various confounders were observed, the relationship between parental/household smoking and respiratory illness in preschool children appeared to vary inversely related to age. Before epidemiologic associations between parental smoking and respiratory health in preschool children can be concluded to reflect any effects of ETS on the respiratory system of these children, it will be necessary to more thoroughly and more consistently consider the role of a number of potential confounding variables, both individually and in combination. It will also be necessary, before reaching such conclusions, to control and/or adjust for these factors where appropriate as well as to more consistently validate parental questionnaire-based clinical endpoints.

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## Introduction

Over the past several years, we have conducted a number of analyses of the literature pertaining to the potential adverse effects of parental and/or household smoking, used as a surrogate for environmental tobacco smoke (ETS) exposure, on the respiratory system and respiratory health of children [1-5]. While an association between parental (usually maternal) smoking and prevalence of acute respiratory symptoms and certain illnesses in pre-school children has been consistently reported in the literature, we found that such an association is much less consistent in studies of school-age or older children. Similarly, we have noted a lack of consistency of association between parental smoking and decreased pulmonary function in older children [1-3]. There have been no relevant studies involving pulmonary function in younger children.

As part of this ongoing analysis, we recently critically and in some detail examined the design of 45 clinical endpoint studies and 38 pulmonary function endpoint studies in school-age and older children. To assist us in this examination, a protocol was developed for the systematic extraction of information from epidemiologic studies [4]. With the aid of this protocol, we considered the following design-related aspects of the studies in question: (1) validation of clinical endpoints that had been obtained largely from parental responses to questionnaires; (2) the frequency with which 21 predetermined, potential confounding variables were considered; (3) criteria used for specific confounding variables, and (4) whether or not specific confounding variables influenced clinical and functional endpoints in these studies.

Our analysis of these studies in school-age and older children revealed that the clinical endpoints, which were usually based upon parental reporting, lacked verification (as from medical records or physician evaluation) in all but 8 of the 45 studies under consideration. In addition, most of the studies considered fewer than half of the 21 potential confounders, while the specific variables that were considered varied widely from study to study. In addition, we found that the criteria used to define a particular variable lacked standardization and varied widely from study to study, most notably for such confounding variables as socioeconomic status (SES), family size, location of residence, age of the subject, active smoking by the subject, outdoor pollution, dampness and cold, type of heating and air-conditioning and quality of housing. Several confounding variables were found to be consistently associated with increased prevalence of respiratory illness

(family and personal health history or male gender) or decreased pulmonary function (personal health history, age, male gender, active smoking and location of residence) [4, 5].

In view of the inconsistencies found in studies of parental/household smoking effects in school age or older children, we initiated a similar analysis of design-related aspects of the parental/household smoking studies in pre-school children. This paper reports our findings to date on this latter analysis.

## Materials and Methods

The 41 studies under examination correspond to those reviewed in a previous report [3]. These studies in preschool children (0-5 years of age) deal only with clinical endpoints (i.e. the prevalence of respiratory symptoms and disease). The 21 potential confounders that were analyzed are listed in table 1. They were derived from the literature, as well as from factors considered intuitively to have a potential direct or indirect effect on the respiratory system. This list is slightly modified from that used previously in school-age children [4, 5], in order to be more relevant to this pre-school age group. Category No. 22 ('others') refers to potential confounders that differed from the 21 predetermined variables.

As indicated previously [4, 5], the studies were reviewed to determine the following information: (1) which of the potential confounders were considered; (2) what parameter(s) was (were) employed for each potential confounder; (3) whether a statistically significant association was looked for between a potential confounder and a clinical endpoint, and, if so, the direction of such an association; (4) whether there was evidence of an interaction between the potential confounder in question and other potential confounders and other variables (including parental/household smoking) that influenced the outcome of the study, and (5) whether clinical endpoints were validated by medical records or a physician's examination.

In order to facilitate the extraction of the foregoing information from the papers in question in a systematic fashion, a computer-assisted protocol was used that was slightly modified from that developed by us and described in our previous studies in school-age or older children [4, 5].

## Results

### *General Consideration of Potential Confounders and Validation of Clinical Endpoints*

As shown in table 1, most of the 21 potential confounding variables were considered in less than half of the 41 relevant studies. The only exceptions to this were (n studies): SES (34), family (26) and subject's personal health history (24), family size (23), residence location (23), age of subject (all 41) and gender (24). Other potential confounding variables were considered in very few of the studies, including indoor pollution other than that

attributed to gas stove usage (5 studies), day care use (6), animal exposures (3), stress (1), dampness and cold (3), nutritional status of the child other than that associated with breast or artificial feeding (1) and maternal smoking during pregnancy (4). Possible exposure of the subjects to occupational contaminants and pollutants carried through the parents was considered in none of the studies. Those potential confounders designated as 'others' (item No. 22, table 1) included age of a sibling, age of parents, family composition, method of paying hospital bill, and mother working during pregnancy. Table 1 also indicates that only 21 of the 41 studies under examination validated clinical endpoints by either medical records or examination by a physician.

Table 2 displays confounder consideration for each of the studies in question and also identifies those studies in which clinical endpoints were validated. This table shows that there is a great deal of variation from one report to the other with regard to the particular array of potential confounders considered (i.e. the distribution of '+' symbols). Table 3 indicates that in all but 3 of the studies [26, 27, 39], 10 or fewer of the confounders were considered.

#### *Detailed Information on Specific Confounding Variables*

As detailed in table 4, a wide variety of criteria were used to characterize SES in the 34 studies that considered this variable. Among these were ownership of an automatic dishwasher, median or taxable income, 'social class', mother's and/or father's occupation, family living standards, mother's marital status, ethnicity, current military status, quality of home equipment (low to luxurious), frequency with which a family moved, presence in the home of both biological parents, and an SES scale based on a number of criteria. Depending upon the study, SES was based either upon a single criterion or several individual criteria.

Table 4 shows that in 10 of the studies [10, 14, 27, 28, 30, 31, 33, 39, 40, 45], no association was observed between an SES parameter and clinical endpoints, while an inverse association was found in 4 studies [19, 23, 29, 34]. One study reported that ethnicity was associated with respiratory illness, where West Indian children had a higher prevalence of chest colds compared to English/Irish or Asian children [40]. One study demonstrated an interaction between maternal work status, maternal smoking and acute respiratory illness [43]. In 8 of the studies [6, 7, 12, 17, 18, 20, 24, 35], the population was stated to have been matched or homogeneous for SES, and, therefore, no data could be provided on the associa-

**Table 1.** Frequency of consideration of potential confounders and validation of respiratory endpoints in epidemiologic studies of parental smoking and respiratory symptoms/diseases in preschool-age children

Confounder No.	Potential confounder or validation of clinical endpoint	Studies <sup>1</sup> (41 total)
1	SES	34
2	Gas fuel usage (cooking and heating)	12
3	Family health history	26
4	Subject's health history	24
5	Infant feeding (breast vs. bottle)	14
6	Outdoor pollution	16
7	Indoor pollution <sup>2</sup>	5
8	Day care use	6
9	Family size	23
10	Animal exposures	3
11	Stress	1
12	Dampness and cold	3
13	Type of heating and presence of air-conditioning	9
14	Season	18
15	Occupational exposure of subject (through parents)	0
16	Quality of housing	9
17	Nutritional status	1
18	Residence location	23
19	Age of subject	41
20	Gender of subject	24
21	Maternal smoking during pregnancy <sup>3</sup>	4
22	Others <sup>4</sup>	9
23	Validation of clinical endpoints <sup>4</sup>	21

<sup>1</sup> Number of studies in which potential confounder was considered or where clinical endpoint was validated.

<sup>2</sup> Other than that attributed to gas stove.

<sup>3</sup> As distinguished from postnatal smoking.

<sup>4</sup> See table 2.

tion between SES and respiratory symptoms and diseases. No information on the association between SES and a clinical endpoint was provided in 11 studies that were, therefore, designated as 'none reported' [8, 9, 11, 16, 21, 22, 26, 36, 37, 41, 46]. In 22 studies [8-11, 14, 16, 19, 21-23, 26, 27, 29, 31, 33, 34, 36, 37, 39, 41, 43, 47], an association observed between parental/household smoking and the prevalence of respiratory symptoms and/or disease was adjusted for SES in some way other than that produced by matching or homogeneity.

**Table 2.** Consideration of potential confounding variables in epidemiologic studies of parental/household smoking and respiratory symptoms/diseases in preschool-age children

Study	Refer- ence	Confounder No. <sup>1</sup>																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
Cameron et al.	6	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	
Cameron and Robertson	7	+	-	-	+	-	+	+	-	+	-	-	-	-	+	-	-	-	+	+	-	-	+ <sup>3,4</sup>	
Colley et al.	8	+	-	+	+	-	+	-	-	+	-	-	-	-	-	-	-	-	+	+	-	-	-	
Harlap and Davies <sup>2</sup>	9	+	-	-	+	-	-	-	-	+	-	-	-	-	+	-	-	-	+	+	-	-	-	
Leeder et al. <sup>2</sup>	10	+	-	+	-	-	+	-	-	+	-	-	-	-	-	-	-	-	+	+	+	-	+ <sup>3</sup>	
Rantakallio <sup>2</sup>	11	+	-	-	+	-	-	-	-	+	-	-	-	-	+	-	-	-	+	+	+	-	-	
Sims et al. <sup>2</sup>	12	+	-	+	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	+	+	-	-	
Dutau et al. <sup>2</sup>	13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	
Speizer et al. <sup>2</sup>	14	+	+	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	+	+	+	-	-	
Dutau et al.	15	-	-	+	-	-	+	-	+	-	-	-	+	+	-	-	+	-	-	+	-	-	-	
Fergusson et al. <sup>2</sup>	16	+	-	-	+	+	-	-	-	+	-	-	-	-	+	-	-	+	+	+	-	-	+ <sup>4,5</sup>	
Pullan and Hey <sup>2</sup>	17	+	-	+	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	+	+	-	-	
Ekwo et al.	18	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	
Schenker et al.	19	+	+	+	-	-	+	-	-	-	-	-	-	-	+	-	-	-	+	+	+	-	-	
Hall et al. <sup>2</sup>	20	+	-	+	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	+	+	-	+ <sup>6</sup>	
Ware et al.	21	+	+	+	-	-	+	-	-	+	-	-	-	+	-	-	-	-	+	+	+	-	-	
Fergusson and Horwood <sup>2</sup>	22	+	-	+	+	+	-	-	-	+	+	+	-	-	-	-	-	-	+	+	+	-	-	
Ferris et al.	23	+	+	+	-	-	+	-	-	+	-	-	-	+	-	-	-	-	+	+	+	-	-	
Pedreira et al. <sup>2</sup>	24	+	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	
Tominaga and Itoh <sup>2</sup>	25	-	+	+	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	
Chen et al.	26	+	-	+	+	+	+	+	-	+	-	-	-	-	-	-	+	-	+	+	+	+	+ <sup>4</sup>	
McConnochie and Roghmann <sup>2</sup>	27	+	+	+	+	+	-	-	+	+	+	-	-	+	+	-	-	-	+	+	+	-	+ <sup>3</sup>	
Park and Kim	28	+	-	+	+	-	-	-	-	+	-	-	-	-	+	-	+	-	+	+	+	-	+ <sup>4</sup>	
Bisgaard et al. <sup>2</sup>	29	+	-	-	+	+	-	-	+	+	-	-	-	-	+	-	+	-	+	+	+	-	-	
Cogswell et al. <sup>2</sup>	30	+	-	+	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	
Fleming et al.	31	+	-	+	-	+	-	-	+	+	-	-	-	-	+	-	-	-	-	+	+	-	-	
Geller-Bernstein et al. <sup>2</sup>	32	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	
Kershaw <sup>2</sup>	33	+	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	
Ogston et al. <sup>2</sup>	34	+	+	-	-	+	-	-	-	+	-	-	-	+	-	-	-	-	-	+	-	-	+ <sup>4,7</sup>	
Salzman et al. <sup>2</sup>	35	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	
Stern et al.	36	+	+	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	
Taylor and Wadsworth	37	+	-	-	+	+	-	-	-	+	-	-	-	-	+	-	+	-	-	+	-	+	-	
Toyoshima et al. <sup>2</sup>	38	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	
Chen et al.	39	+	+	+	+	+	+	+	+	+	-	-	-	-	+	-	+	-	+	+	+	+	+ <sup>3</sup>	
Marks	40	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	
Chen	41	+	-	-	+	+	+	-	-	-	-	-	-	-	+	-	-	-	+	+	+	+	-	
Murray and Morrison	42	-	+	+	+	-	-	+	-	-	+	-	-	+	-	-	-	-	-	+	+	-	-	
Ostro	43	+	-	+	+	-	+	-	-	+	-	-	+	-	+	-	-	-	+	+	+	-	-	
Harsten et al. <sup>2</sup>	44	-	-	+	-	-	+	-	+	+	-	-	-	-	+	-	+	-	+	+	+	-	-	
Ross et al. <sup>2</sup>	45	+	+	+	+	-	-	-	-	+	-	-	-	+	+	-	-	+	-	+	+	-	-	
Weitzman et al.	46	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	+	+	-	-

+ = Indicates that potential confounding variables were considered in a particular study.

<sup>1</sup> Corresponds to numbers in table 1.

<sup>2</sup> Clinical endpoints verified.

<sup>3</sup> Age of sibling.

<sup>4</sup> Age of parent.

<sup>5</sup> Family composition.

<sup>6</sup> Method of paying hospital bill.

<sup>7</sup> Mother working during pregnancy.

**Table 3.** Number of individual/potential confounders considered in each of the epidemiologic studies

Study	Reference	Confounders considered (out of a possible 22 <sup>1)</sup> )
Cameron et al.	6	4
Cameron/Robertson	7	9
Colley et al.	8	7
Harlap/Davies	9	6
Leeder et al.	10	8
Rantakallio	11	7
Sims et al.	12	7
Dutau et al.	13	1
Speizer et al.	14	7
Dutau et al.	15	7
Fergusson et al.	16	9
Pullan and Hey	17	7
Ekwo et al.	18	4
Schenker et al.	19	8
Hall et al.	20	8
Ware et al.	21	9
Fergusson and Horwood	22	10
Ferris et al.	23	9
Pedreira et al.	24	5
Tominaga and Itoh	25	5
Chen et al.	26	13
McConnochie and Roghmann	27	14
Park and Kim	28	10
Bisgaard et al.	29	10
Cogswell et al.	30	6
Fleming et al.	31	8
Geller-Bernstein et al.	32	4
Kershaw	33	5
Ogston et al.	34	7
Salzman et al.	35	3
Stern et al.	36	6
Taylor and Wadsworth	37	8
Toyoshima et al.	38	4
Chen et al.	39	16
Marks	40	3
Chen	41	9
Murray and Morrison	42	8
Ostro	43	10
Harsten et al.	44	9
Ross et al.	45	10
Weitzman et al.	46	5

<sup>1)</sup> As listed in table 1.

Table 5 details the treatment of family health history as a potential confounding variable. Among the criteria used for this variable were: parental respiratory disability based upon morning phlegm production in winter; sibling respiratory symptoms and diseases; family history of atopy and wheezing; parental cough; exclusion of subjects

on the basis of a disturbed family background; history of wheeze in first degree relatives; parental history of bronchitis, emphysema and asthma; history of asthma, allergic rhinitis and eczema in parents and siblings; adult chronic respiratory disease in the family; number of sick children in the household; family history of acute otitis media, and recent family history of respiratory infection.

Table 5 shows that in 6 of the studies [12, 17, 18, 20, 31, 38], no association was observed between family health history and clinical endpoints, while a direct association was observed in 12 studies [8, 10, 15, 19, 21, 23–25, 27, 28, 33, 43]. A possible interaction was noted between maternal smoking and family health history in 1 study [25]. In 2 studies [30, 42], the population was matched or considered homogeneous for family health history and, thus, provided no data on associations. In 6 studies [22, 26, 36, 39, 44, 45], no information regarding associations of the endpoint and family health history was provided ('none reported'). In 12 studies [8, 10, 18, 19, 21–23, 26, 27, 36, 39, 43], the observed association between parental smoking and prevalence of respiratory symptoms and diseases in children was adjusted for family health history in some way other than that produced by homogeneity or matching.

Details regarding the treatment of personal health history as a potential confounder are provided in table 6. Among the specific criteria for this potential confounder were illness in the past year, birth weight, birth order, history of respiratory syncytial virus (RSV) bronchiolitis or RSV infection, gestational age, perinatal status, early eczema, early respiratory illness, birth interval, atopic history, body fluid immunoglobulins, history of lower respiratory tract infections, history of hospital admissions for chest problems, pertussis immunization status, eosinophilia history, and previous attacks of acute otitis media. While no association with respiratory symptoms and diseases was observed in 4 studies [16, 26, 33, 38], a direct association was found in 8 studies [9, 17, 20, 22, 29, 30, 32, 38]. An interaction between low birth weight, other variables and household smoking is suggested in another study [39]. No data could be provided on associations relative to this variable in 5 studies [6, 7, 12, 27, 42] because populations were either matched or considered homogeneous. No information on the influence of personal health history on respiratory illness was reported in 6 of the studies [8, 28, 37, 41, 43, 45]. In 8 studies that reported an association between parental/household smoking and clinical endpoints [8, 9, 30, 32, 37, 39, 40, 43], adjustment was made for personal health history of the subject in some way other than that of matching and homogeneity.

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**Table 4.** Consideration of SES in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Cameron et al.	6	automatic dishwasher	NA (matched)
Cameron and Robertson	7	median yearly income	NA (matched)
Colley et al.	8	social class	none reported
Harlap and Davies	9	husband's occupation	none reported
Leeder et al.	10	father's occupation	none observed
Rantakallio	11	father's occupation; taxable income of families; matched for marital status of mother	none reported
Sims et al.	12	social class based on occupation	NA (matched)
Dutau et al.	13	none	NA
Speizer et al.	14	educational attainment and occupation of both parents	none observed
Dutau et al.	15	none	NA
Fergusson et al.	16	education; family living standards; maternal ethnic status; family income	none reported
Pullan and Hey	17	social class	NA (matched)
Ekwo et al.	18	subjects were from middle and upper social classes	NA (homogeneous)
Schenker et al.	19	SES scale based on parental occupation and education; sample was 98% white	severe chest illness before 2 years of age inversely related to SES
Hall et al.	20	cases and controls matched for race	NA (matched)
Ware et al.	21	parental occupation and education; Green SES scale based on income, occupation, ethnicity and maternal education	none reported
Fergusson and Horwood	22	Elley and Irving scale (which incorporates maternal age, family size, maternal educational level, children's ethnicity, and social and economic status of family)	none reported
Ferris et al.	23	three levels of SES based on mean number of years of schooling of the parents	respiratory illness before the age of 2 years is inversely related to SES
Pedreira et al.	24	89% of subjects were white	NA (homogeneous)
Tominaga and Itoh	25	none	NA
Chen et al.	26	family income; father's education	none reported
McConnochie and Roghmann	29	subject population primarily composed of white middle-class families; dichotomous SES index based upon level of maternal education	none observed
Park and Kim	28	father's occupation; parental education; economic status (upper, middle, lower)	none observed

2023510619

Table 4 (continued)

Study	Reference	Parameter(s)	Associations
Bisgaard et al.	29	social status scale based on occupation, salary, education, and type of living accommodation	low social status score a risk factor for wheeze in infancy
Cogswell et al.	30	social class	none observed
Fleming et al.	31	ethnicity; family income	none observed
Geller-Bernstein et al.	32	none	NA
Kershaw	33	civilian vs. armed service	none observed
Ogston et al.	34	father's employment (manual vs. nonmanual)	respiratory and alimentary illnesses inversely related to social class
Salzman et al.	35	matched for ethnicity	NA (matched)
Stern et al.	36	study locales of similar demographic and economic profiles; adjusted for parental education	none reported
Taylor and Wadsworth	37	assessment of home equipment by health visitor (luxurious, high, average, low, very low standard); number of times family moved during child's life; social index (based on domestic crowding, parental education, tenure of accommodation, type of neighborhood, parental occupation)	none reported
Toyoshima et al.	38	none	NA
Chen et al.	39	father's educational status (university, secondary, primary); average living costs per capita	none observed
Marks	40	ethnicity (English/Irish, Asian, West Indian)	none observed for wheezing, coughing; West Indian children had significantly higher incidence of chest colds
Chen	41	annual income; father's education (university, secondary, primary)	none reported
Murray and Morrison	42	none	NA
Ostro	43	education of head of household; family income; work status of mother; ethnicity	positive interaction between maternal smoking and nonworking mother and acute respiratory illness
Harsten et al.	44	none	NA
Ross et al.	45	social class based upon occupation; number of parents/adults in house	none observed
Weitzman et al.	46	race; presence of both biological parents; family income; maternal education (less than high school, high school, college)	none reported



**Table 5.** Consideration of family health history in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Cameron et al.	6	none	NA
Cameron and Robertson	7	none	NA
Colley et al.	8	parental respiratory disability based upon morning phlegm production in winter	incidence of bronchitis and pneumonia at 1 year of age associated with parental symptoms; association disappears at 2-5 years
Harlap and Davies	9	none	NA
Leeder et al.	10	parents (morning phlegm in winter; asthma-wheeze); siblings (cough-phlegm, bronchitis, pneumonia, colds, whooping cough, etc.)	incidence of bronchitis and pneumonia at 1 year of age associated with parental asthma-wheeze and sibling bronchitis and pneumonia; incidence of upper respiratory illness (bad colds) at 1 year of age associated with parental cough-phlegm and sibling bronchitis and pneumonia
Rantakallio	11	none	NA
Sims et al.	12	family history of atopy and wheezing	none observed
Dutau et al.	13	none	NA
Speizer et al.	14	none	NA
Dutau et al.	15	parental coughing	parental coughing associated with coughing in children
Fergusson et al.	16	none	NA
Pullan and Hey	17	exclusion of subjects on the basis of disturbed family background; history of wheeze in first degree relatives	none observed
Ekwo et al.	18	parental respiratory history	none observed
Schenker et al.	19	parental respiratory and allergic history	parental history associated with severe chest illness in children < 2 years of age
Hall et al.	20	family history of atopy (allergic rhinitis, asthma)	none observed
Ware et al.	21	history of bronchitis, emphysema, or asthma of either parent	parental history strong risk factor for respiratory illness in children < 2 years of age
Fergusson and Horwood	22	history of asthma, allergic rhinitis, and eczema in parents and siblings	none reported
Ferris et al.	23	history of bronchitis, emphysema, or asthma of either parent	parental history of respiratory illness associated with respiratory illness < 2 years of age
Pedreira et al.	24	family history of chronic cough, chronic bronchitis, asthma, other respiratory illness	family history of cough and bronchitis are associated with increased bronchitis (but not tracheitis) in infants; family history of asthma or other respiratory illnesses not associated with bronchitis or tracheitis in infants
Tominaga and Itoh	25	family history of cough and sputum	associated with common colds (but not asthmatic bronchitis) in 3-year-olds; possible interaction with maternal smoking for asthmatic bronchitis
Chen et al.	26	adult cases of chronic respiratory disease in family	not reported

Table 5 (continued)

Study	Reference	Parameter(s)	Associations
McConnochie and Roghmann	27	history of hay fever (and/or allergic rhinitis) or asthma in parents and/or siblings	family history of asthma (but not allergy) risk factor for bronchiolitis
Park and Kim	28	cough and phlegm in household	cough in household associated with cough in children
Bisgaard et al.	29	none	NA
Cogswell et al.	30	all children had a parental history of asthma or hay fever	NA (homogeneous)
Fleming et al.	31	number of children sick within household	none observed
Geller-Bernstein et al.	32	none	NA
Kershaw	33	family history of atopic symptoms in first degree relatives	predictor of asthma
Ogston et al.	34	none	NA
Salzman et al.	35	none	NA
Stern et al.	36	history of chronic respiratory illness in either parent	none reported
Taylor and Wadsworth	37	none	NA
Toyoshima et al.	38	major allergy (atopic dermatitis, asthma, rhinitis, recurrent urticaria) and minor allergy (adverse drug reaction) in relatives	none observed
Chen et al.	39	adult history of chronic respiratory disease	none reported
Marks	40	none	NA
Chen	41	none	NA
Murray and Morrison	42	exposed and nonexposed children comparable with regard to family history of asthma	NA (matched)
Ostro	43	parental respiratory illness	significantly associated with days children spent in bed due to respiratory illness
Harsten et al.	44	family history of allergy (eczema, asthma, hay fever, nettle rash, drug allergy) and acute otitis media	none reported
Ross et al.	45	recent family history of respiratory infection	none reported
Weitzman et al.	46	none	NA

As shown in table 7, the following specific criteria were used to characterize infant feeding as a confounding variable: early infant diet; presence or absence of breast feeding; duration of breast feeding; method of infant feeding (breast, mixed, artificial); time of initiation of formula, whole milk and solid food; age of weaning, and formula use after 1 month of age. No association between the endpoint and infant feeding was observed in 7 studies [20, 27, 29, 30, 31, 34, 38]. A direct association between artificial

feeding and increased prevalence of respiratory symptoms and/or certain diseases in children (or an inverse relationship of the endpoint with breast feeding) was noted in 2 studies [26, 32]. In 2 studies, infant feeding appeared to interact with other confounding variables and/or household smoking [39, 41]. No information pertaining to an association between this variable and endpoints was reported in 3 studies [16, 22, 37]. The association between parental/household smoking and prevalence

**Table 6.** Consideration of subject's personal health history in the epidemiologic studies.

Study	Reference	Parameter(s)	Associations
Cameron et al.	6	no difference between exposed and nonexposed subjects with regard to illness within the past year	NA (matched)
Cameron and Robertson	7	stated that most of the children were not ill	NA (homogeneous)
Colley et al.	8	subjects from multiple births excluded from study; birth weight	none reported
Harlap and Davies	9	birth weight; birth order	admission rates for respiratory illnesses are elevated in infants with low birth weights
Leeder et al.	10	none	NA
Rantakallio	11	birth order of exposed and nonexposed subjects matched	NA
Sims et al.	12	cases (RSV bronchiolitis) and controls matched for birth weight and atopic history	NA (matched)
Dutau et al.	13	none	NA
Speizer et al.	14	none	NA
Dutau et al.	15	none	NA
Fergusson et al.	16	birth weight; gestational age	none observed
Pullan and Hey	17	subjects excluded from the study on the basis of physical handicap (spina bifida, tracheoesophageal fistula, cyanotic congenital heart disease, myopathy, leukemia) severe enough to interfere with assessment; history of RSV infection during 1st year of life	RSV infection associated with wheeze at 0-4 years of age
Ekwo et al.	18	none	NA
Schenker et al.	19	none	NA
Hall et al.	20	subjects were excluded from the study on the basis of underlying disease other than RSV; age of hospitalization for RSV lower respiratory tract disease	younger age ( $\leq 12$ weeks) at time of hospitalization for RSV disease associated with lower arterial $O_2$ at 4-5 years of age
Ware et al.	21	none	NA
Fergusson and Horwood	22	perinatal status (birth weights, gestational ages) early eczema; early respiratory illness	respiratory illness at 0-2 years of age associated with same at 2-4 and 4-6 years of age
Ferris et al.	23	none	NA
Pedreira et al.	24	none	NA
Tominaga and Itoh	25	none	NA
Chen et al.	26	birth weight; relatively few (2-3%) multiple births; children excluded on basis congenital heart disease and death before 18 months of age	none observed for birth weight

Table 6 (continued)

Study	Reference	Parameter(s)	Associations
McConnochie and Roghmann	27	cases (bronchiolitis) and controls excluded for medical abnormalities (premature birth, cardiac anomaly, neuromuscular disorder, esophageal atresia)	NA (homogeneous)
Park and Kim	28	birth order; birth interval	none reported
Bisgaard et al.	29	birth weight	low birth weight (<2,500 g) associated with increased wheezing during the 1st year of life
Cogswell et al.	30	atopic history (eczema or skin prick test); body fluid IgE and IgA	atopic history associated with wheezing in children; IgE (but not IgA) associated with wheeze
Fleming et al.	31	none	NA
Geller-Bernstein et al.	32	history of lower respiratory tract infections; blood IgE; all were atopic by skin test	history of respiratory illness negatively correlated with recovery of persistent wheeze; none observed for IgE
Kershaw	33	previous hospital admissions for chest problems; pertussis immunization status; chest deformity; evidence of atopy and/or atopic potential; serum IgE	none observed for IgE and pertussis immunization, and chest deformity; none reported hospitalization history
Ogston et al.	34	none	NA
Salzman et al.	35	none	NA
Stern et al.	36	none	NA
Taylor and Wadsworth	37	birth weight; birth order	none reported
Toyoshima et al.	38	serum IgE; eosinophilia history (and age of initial wheezing); allergic history (eczema, allergic rhinitis, recurrent urticaria, food allergy); disturbances at birth; fever with wheezing	eosinophilia found in asthmatic infants more than in nonasthmatic infants; age of initial wheezing in asthmatic infants significantly older than in nonasthmatic infants; none observed for other variables
Chen et al.	39	preterm birth; birth weight	low birth weight (along with artificial feeding and male gender) may enhance association between household smoking and hospitalization due to respiratory illness during the first 18 months of life
Marks	40	none	NA
Chen	41	birth weight; multiple births	none reported
Murray and Morrison	42	all asthmatics; exposed and nonexposed matched for number and duration of colds, atopy (by skin test); size of mite reaction larger in exposed than in nonexposed subjects	NA (matched)
Ostro	43	existence of chronic health conditions	none reported
Harsten et al.	44	none	NA
Ross et al.	45	number of previous attacks of acute otitis media	none reported
Weitzman et al.	46	none	NA

**Table 7.** Consideration of breast versus bottle feeding of infants in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Fergusson et al.	16	early infant diet	none reported
Hall et al.	20	breast feeding	none observed
Fergusson and Horwood	22	presence, absence and duration of breast feeding	none reported
Chen et al.	26	method of infant feeding (breast or mixed vs. artificial)	artificial feeding predictor of hospital admissions for respiratory infections in children $\leq 18$ months
McConnochie and Roghmann	27	breast feeding (occurrence and duration) and time of initiation of formula, whole milk and solid food	none observed
Bisgaard et al.	29	age of weaning from breast	none observed
Cogswell et al.	30	duration of breast feeding	none observed
Fleming et al.	31	breast feeding in children $< 6$ months of age	none observed
Geller-Bernstein et al.	32	breast feeding	inversely associated with persistence of wheeze
Ogston et al.	34	bottle vs. breast feeding	none observed upon regression analysis
Taylor and Wadsworth	37	breast feeding	none reported
Toyoshima et al.	38	use of formula after 1 month of age	none observed
Chen et al.	39	breast/mixed feeding vs. artificial feeding	artificial feeding (along with male gender and low birth weight) may enhance association between household smoking and hospitalization due to respiratory illness during the first 18 months of life
Chen	41	breast/mixed feeding vs. artificial feeding	artificial feeding enhanced dose-response relationship between household smoking and incidence of hospitalization due to respiratory illness during the first 18 months of life

of respiratory symptoms and disease in preschool children was adjusted for infant feeding in some way other than by matching or homogeneity in 4 studies [16, 22, 26, 37].

As detailed in table 8, the specific criteria for day care use were: home care vs. day care and kindergarten; day care outside the home; and home care vs. family care vs. a day-care center. The population was considered homogeneous for this variable in 1 study [27], and was omitted from the regression model in another [39]. A direct association between day care and the prevalence of respiratory symptoms and/or disease was reported in 4 studies [5, 29, 31, 44]. The observed association between parental household smoking and endpoint was adjusted for this variable in 2 studies [29, 31].

Table 9 provides details on 4 potential confounding variables: (a) gas fuel usage; (b) indoor pollution other than gas fuel usage; (c) dampness and cold, and (d) type of heating and air-conditioning. The criteria used for gas fuel usage were gas fuel usage, gas cooking fuel, cooking stoves, home cooking fuel, and gas for cooking and heating. This variable was matched in 1 study [42]. No association for gas fuel usage and the endpoint was observed in 4 studies [19, 21, 25, 34], while gas fuel use was associated with the prevalence of respiratory symptoms and disease in 3 studies [4, 18, 45]. No information regarding associations of the endpoint and gas fuel usage was reported in 4 studies [23, 27, 36, 39]. The observed association between parental/household smoking and incidence of respiratory illness was adjusted for gas fuel usage

**Table 8.** Consideration of day care use in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Dutau et al.	15	home care vs. day care and kindergarten	respiratory index (rating based upon 6 parameters of respiratory illness) elevated in children (1 month–6 years) who go to day care or kindergarten compared to those cared at home
McConnochie and Roghmann	27	none of the subjects were in day care during the study period (first 2 years of life)	NA (homogeneous)
Bisgaard et al.	29	day care outside of the home	day care outside of the home associated with increased wheezing during the 1st year of life
Fleming et al.	31	day care (defined as supervised care of at least 2 unrelated children (> 4 h/week))	associated with increased upper respiratory infection and ear infection in children < 5 years of age
Chen et al.	39	use of day care	omitted from regression model
Harsten et al.	44	home care vs. family day care (4–6 children) vs. day care centers (10–12 children)	select forms of respiratory tract infection elevated in 2- and 3-year olds attending day care centers relative to family day care and home care

in 2 studies [6, 25]. A potential interaction between parental smoking and this variable was reported in another study [18] (table 9).

The criteria used for indoor pollution other than gas stove usage were: ventilation problems; quality of ventilation; kerosene stove; ventilated heater; coal for cooking, and woodstove emissions. Two studies were matched for indoor pollution [7, 42]. No association with the endpoint was observed in 1 study [25], and no information on an association was reported in 2 studies [26, 39]. The observed association between parental smoking and the endpoint was adjusted for indoor pollution in 1 study [25] (table 9).

The criteria used for dampness and cold were: cold temperature; relative humidity; temperature in the bedroom and living room; the absence of a radiator in the bedroom, and minimum winter temperature. No association was observed for cold in 1 study [15], while in another study respiratory illness in children was associated with cooler, more humid bedrooms [45]. No information concerning associations attributable to this variable was available in 1 study [43]. In this particular study, the effect associated with ETS was adjusted for this variable [43] (table 9).

The specific criteria used for type of heating and air-conditioning were: type of heating (oil, gas, electric); heat-

ing fuel and air-conditioning; presence of an air conditioner; home heating methods; wood stove use, and gas vs. central heating. This potential confounding variable was matched in 1 study [42]. No association between this variable and endpoint was observed in 3 studies [14, 21, 23], while an association was observed in 4 studies [15, 25, 34, 45]. No information regarding an association was available in 1 study [27]. An observed association between parental smoking and the endpoint was adjusted for this variable (other than by matching) in 1 study [34] (table 9).

Table 10 deals with the treatment of gender as a potential confounding variable. This variable was matched in 1 study [12]. No association between gender and respiratory illness was observed in 5 studies [19, 28, 31, 32, 44], while in 8 studies [10, 17, 21, 23, 27, 29, 33, 41], male gender was associated with increased prevalence of respiratory illness. An interaction between male gender and other variables and household smoking was suggested in 1 study [39]. In no study was such an association found for female gender. No information was available for gender as a potential variable in 9 studies [6, 11, 14, 20, 22, 26, 42, 43, 46]. Observed associations between parental/household smoking and respiratory illness were adjusted for gender (other than by matching) in 5 studies [10, 21, 29, 41, 42].

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**Table 9.** Consideration of gas fuel usage, indoor pollution, dampness and cold, and type of heating and presence of air-conditioning in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Cameron and Robertson	7	B) percent reporting ventilation problems similar for exposed vs. nonexposed households	NA (matched)
Speizer et al.	14	A) gas fuel usage (monitored mass respirable particles and NO <sub>2</sub> ) D) type of heating (oil, gas, electric)	A) associated with serious respiratory illness before age of 2 years D) none observed
Dutau et al.	15	C) cold temperature D) collective vs. individual heating	C) none observed D) collective heating associated with increased respiratory illness
Ekwo et al.	18	A) gas cooking fuel	A) associated with increased risk of hospitalization for respiratory illness before 2 years of age
Schenker et al.	19	A) cooking stove fuel (gas electric or other)	A) none observed
Ware et al.	21	A) use of gas cooking D) heating fuel and air-conditioning	A) none observed D) dropped from regression analysis because it did not figure into regression
Ferris et al.	23	A) use of gas cooking D) heating fuel and air-conditioning	A) none reported D) dropped from regression analysis because it did not figure into regression
Tominaga and Itoh	25	A) gas stoves B) kerosene stove, electric stove, ventilated heater D) air conditioner	A) none observed B) none observed D) associated with increased common colds in 3-year olds
Chen et al.	26	B) coal used for cooking	B) none reported
McConnochie and Roghmann	27	A) home cooking fuel D) home heating methods	A) none reported D) none reported
Ogston et al.	34	A) gas cooking and heating D) type of heating (e.g. coal, gas, electric, etc.)	A) none observed for gas cooking D) respiratory illness during 1st year of life associated with type of heating (gas and electric > central storage and coal)
Stern et al.	36	A) gas cooking in the home	A) none reported
Chen et al.	39	A) cooking fuel (coal, gas) B) ventilation in home (good, fair, bad)	A) none reported B) none reported
Murray and Morrison	42	A) exposed and nonexposed children were comparable for gas stove usage B), D) exposed and nonexposed children were comparable for emissions for woodstove use for heating	A) NA (matched) B), D) NA (matched)
Ostro	43	C) winter minimum temperature	none reported
Ross et al.	45	A) gas use for heating and cooking C) mean relative humidity and temperature in bedroom and living room; central heating radiator vs. no heating in child's bedroom D) gas vs. central heating	A) see D) C) upper respiratory infection in children 3-5 years old associated with cooler bedrooms and higher relative humidity D) wheezing associated with gas vs. central heating in children 3-5 years old

A) = Gas fuel usage; B) = indoor pollution; C) = dampness/cold; D) = type of heating/presence of air-conditioning.

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**Table 10.** Consideration of gender in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Cameron et al.	6	exposed and nonexposed children matched for gender	none reported
Leeder et al.	10	gender	bronchitis/pneumonia of males > females in children < 5 years of age
Rantakallio	11	exposed and nonexposed children matched for gender	none reported
Sims et al.	12	cases (RSV bronchiolitis) and controls matched for gender	NA (matched case-control)
Speizer et al.	14	gender	none reported
Pullan and Hey	17	cases (RSV infection) and controls matched for gender	episodes of wheeze in boys > girls (0-2 years); none observed for recurrent wheeze
Schenker et al.	19	gender	none observed for chest illness in children < 2 years of age
Hall et al.	20	cases (RSV infection) and controls matched for gender	none reported
Ware et al.	21	gender	males > females for respiratory illness before 2 years of age
Fergusson and Horwood	22	gender	none reported
Ferris et al.	23	gender	males > females for respiratory illness before 2 years of age
Chen et al.	26	gender	none reported
McConnochie and Roghmann	27	cases (bronchiolitis) and controls matched for gender	incidence of bronchiolitis up to 2 years of age in males > females
Park and Kim	28	gender	none observed
Bisgaard et al.	29	gender	incidence of wheezing at 1 year of age in males > females
Fleming et al.	31	gender	none observed
Geller-Bernstein et al.	32	gender	none observed
Kershaw	33	gender	majority of asthmatics ≤ 3 years of age were males
Chen et al., 1988	39	gender	male gender (along with low birth weight and artificial feeding) may enhance association between household smoking and hospitalization due to respiratory illness during the first 18 months of life
Chen	41	gender	frequency of hospitalization due to respiratory illness at 18 months of age in males > than females
Murray and Morrison	42	gender	none reported
Ostro, 1989	43	gender	none reported
Harsten et al., 1990	44	gender	none observed
Weitzman et al., 1990	46	gender	none reported



Table 11. Consideration of age of the subject in the epidemiologic studies

Study	Reference	Parameter(s)	Associations
Cameron et al.	6	< 16, < 9 and < 5 years of age	no age analysis within preschool-age group
Cameron and Robertson	7	0-5, 6-9, 10-16 years of age	no age analysis within preschool-age group
Colley et al.	8	0-5 years, longitudinal study	association between bronchitis and pneumonia in children and parental smoking or parental phlegm disappears by 2 years of age
Harlap and Davies	9	age in months during 1st year of life	association between smoke exposure and admission rates for bronchitis/pneumonia observed at 6-9 months but not 0-5 months of age
Leeder et al.	10	1st year of life	NA (homogeneous)
Rantakallio		compared subjects < 1 year of age with those 1-5 years of age	the 'dose-response' relationship between maternal smoking and respiratory diseases in children < 1 year of age was not demonstrable in children 1-5 years old (although maternal smoking association observed for both age groups)
Sims et al.	12	1st year of life	NA (homogeneous)
Dutau et al.	13	compared those children aged 1-12 months with total group < 6 years of age	at 1-12 months of age prevalence of chronic cough less than, while prevalence of asthmatooid bronchitis, rhinopharyngitis, and laryngitis more than total group (all children were smoke-exposed with no unexposed control children); total number of children is small (n = 40)
Speizer et al.	14	respiratory illness in children < 2 years old was one of the endpoints	NA (homogeneous)
Dutau et al.	15	11 month-6 years of age	no age comparisons within this age group
Fergusson et al.	16	1, 2, 3 years of age	association between maternal smoking and bronchitis/pneumonia disappears by 3 years of age
Pullan and Hey	17	10-year longitudinal study; history of wheeze from 0-4 years of age was an endpoint	no age comparison within this age group
Ekwo et al.	18	hospitalization for respiratory illness before age 2 was one of the endpoints	NA (homogeneous)
Schenker et al.	19	severe chest illness prior to 2 years of age was one of the endpoints	NA (homogeneous)
Hall et al.	20	8-year longitudinal study of subsequent effects of infantile RSV infection	no age comparison within preschool-age group
Ware et al.	21	respiratory illness before 2 years of age was one of the endpoints	NA (homogeneous)
Fergusson and Horwood	22	6-year longitudinal study	rates of respiratory symptoms and illness higher in children 0-2 years old compared to those 2-6 years of age; association between maternal smoking and lower respiratory symptoms and infection in children disappeared after 2 years of age
Ferris et al.	23	respiratory illness before 2 years of age was one of the endpoints	NA (homogeneous)
Pedreira et al.	24	1st year of life	NA (homogeneous)
Tominaga and Itoh	25	all children 3 years of age	NA (homogeneous)
Chen et al.	26	0-18 months of age	NA (homogeneous)

Table 11 (continued)

Study	Reference	Parameter(s)	Associations
McConnochie and Roghmann	27	cases (bronchiolitis) and controls matched for age; retrospective study involving all children < 2 years of age	NA (matched and homogeneous)
Park and Kim	28	0–14 years of age	no separate evaluation within preschool-age group
Bisgaard et al.	29	1st year of life	NA (homogeneous)
Cogswell et al.	30	longitudinal study in children 0–5 years of age with a genetic predisposition to allergic disease	majority (69%) of children had 1st episode of wheezing by 2 years of age; during the 1st year of life ingested allergen accounted for most of the (+) atopic reactions in children with eczema while at age 5 inhalant allergens were the predominant cause of (+) atopic reaction in children with eczema; parental smoking associated with wheeze at 5 years of age but not at 1 year of age
Fleming et al.	31	0–5 years of age (comparison above and below 36 months of age)	children < 36 months were at greater risk of ear infection than children > 36 months old; household crowding increases risk of upper respiratory tract infection in children < 36 months old
Geller-Bernstein et al.	32	≤ 5 years of age	no age comparisons in this group
Kershaw	33	≤ 6 years of age	no age comparison in this group
Ogston et al.	34	within 1st year of life	NA (homogeneous)
Salzman et al.	35	cases (croup) and controls matched for age; children < 5 years old vs. children < 1 year old	none reported
Stern et al.	36	hospitalization for chest illness before the age of 2 was one of the endpoints	NA (homogeneous)
Taylor and Wadsworth	37	0–5 years of age, all subjects born at the same time; comparison of hospital admission for lower respiratory illness at 0–12, 12–35 and 35–59 months	association between maternal smoking and hospital admissions for lower respiratory illness greatest at 0–12 months of age
Toyoshima et al.	38	0–3 years of age; average age between cases (asthma) and 2 sets of controls (wheezy, nonwheezy) were not significantly different	matched; however, initial age of wheezing for asthma group was significantly later than for controls
Chen et al.	39	0–18 months of age; comparison of infants 0–6 months old with those 7–18 months old	association between household smoking and incidence of hospitalization due to respiratory illness declines at 7–18 months compared to 0–6 months of age
Marks	40	all children 4.5–5 years of age	NA (homogeneous)
Chen	41	0–18 months of age	NA (homogeneous)
Murray and Morrison	42	one of the age groups compared for asthma severity was 1–6 years of age	no comparison made within this age group
Ostro	43	0–6 years of age; adjusted for age	none reported
Harsten et al.	44	0–3 years of age; endpoints analyzed on the basis of quarters	selected respiratory diseases and ear infection more prevalent during year 2 than years 1 and 3; incidence of acute tonsillitis greater in years 2 and 3 than year 1; see table 8 for additional age-related associations
Ross et al.	45	3–5 years of age	NA (homogeneous)
Weitzman et al.	46	0–5 years of age; examined asthma onset at 1 year and 2–5 years	none reported

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Table 11 shows that a wide variation of age ranges (i.e. <3, 0-4, 0-5, 0-6 and 0-14 years, <1 year, <2 years, 1 month-6 years, 3 years of age and 4.5-5 years) and age comparisons (i.e. 0-5 vs. 6-9 months, 1-12 months vs. <6 years, 0-2 vs. 2-6 years, above and below 36 months, <1 vs. <5 years) were considered in the 41 relevant studies. Ages were matched or subjects were homogeneous for age in 17 studies [10, 12, 14, 18, 19, 21, 23-25, 27, 29, 34, 36, 38, 40, 41, 45]. An association between age and the endpoint was observed in 7 studies [11, 13, 22, 30, 31, 38, 44]. Of these, prevalence of respiratory illness and disease was inversely associated with age in 5 studies [13, 22, 31, 38, 44] and directly associated with age in 3 studies [13, 30, 44]. A biphasic age-related association was found in 2 studies [13, 44]. An interaction between age and day care use is suggested in 1 study [42], while another study suggests an interaction between age and crowding [31]. An interaction between age and parental/household smoking is suggested in six studies [8, 9, 11, 16, 37, 39], with all but 1 [9] showing that this association diminished with age. No information regarding an association between age and end point was provided in 12 studies [6, 7, 15, 17, 20, 28, 32, 33, 35, 42, 43, 46]. In 5 studies where an association between parental/household smoking and respiratory symptoms and illness was reported [8, 22, 31, 37, 38], adjustment was made for age of the subject other than by matching or homogeneity. In 1 study [30], an interaction was suggested between parental smoking, age and wheeze.

The population was matched or considered homogeneous for season as a potential confounding variable in 11 studies [7, 12, 16, 17, 19, 20, 27, 31, 37, 39, 41] (data not shown). Season was associated with clinical endpoints in 3 studies [9, 11, 43] where the prevalence of respiratory illness was greater in winter than at other times of year. In 1 study [30], no association was observed for this variable. In 1 study [29], the risk of wheezing during the first year of life was greater for children born during April-September (spring-fall) than those born during October-March (fall-winter) [29], while in another study, no association was seen for season of birth [30]. In 1 study [43], no information was provided regarding associations between season and respiratory illness. Three studies [9, 11, 29] suggested that season or season of birth has little or no influence on the association between parental/household smoking and endpoint (data not shown).

Table 12 summarizes the associations between the foregoing potential confounding variables and the clinical endpoints in these studies. As can be seen from the table, there was an association between the potential confound-

**Table 12.** Associations between potential confounding variables and clinical endpoints in the epidemiologic studies

Increased/decreased prevalence of symptoms/illness <sup>1</sup>
Family health history (+, 12/18 studies)
Age (-, 5/6 studies)
Gender (+ males, 8/13 studies)
Personal health history (+ 8/12 studies)
Day care use (+, 4/4 studies)
Season (+ winter, 3/4 studies)
No association observed <sup>2</sup>
SES (10/14 studies)
Artificial feeding (7/9 studies)
Gas fuel use/indoor pollution (5/8 studies)
Association equivocal <sup>3</sup>
Dampness and cold (+1 study, no association 1 study)
Heating/air-conditioning (+4 studies, no association 3 studies)

<sup>1</sup> Number of studies with increased (+) or decreased (-) prevalence/total number of studies addressing potential confounder, excluding studies in which groups were homogeneous or the variable was matched or associations not reported.

<sup>2</sup> Number of studies in which no association observed/total number of studies addressing potential confounder, excluding studies in which the groups were homogeneous or the variable was matched or association not reported.

<sup>3</sup> + = increased prevalence of symptoms/illnesses associated with variable.

er and symptoms and/or illness prevalence in a majority of the studies relative to family health history (12 of 18 studies), age (5 of 6), gender (8 of 13), personal health history (8 of 12), day care use (4 of 4) and season (3 of 4). On the other hand, a majority of the studies observed no association relative to SES (10 of 14 studies), artificial feeding (7 of 9) and gas fuel use and indoor pollution other than gas fuel (5 of 8). In the case of dampness and cold and heating/air-conditioning, the data were inconclusive.

## Discussion

In this analysis, we used basically the same systematic protocol employed previously in studies of school-age children to extract information from epidemiologic studies of parental smoking and respiratory health in preschool children. Only 2 modifications were implemented. Confounder No. 21 in the original study, 'active smoking in subjects', was replaced by 'maternal smoking during pregnancy'. It was considered unlikely that active

smoking would be a confounding variable in children under 5 years of age and none of the studies considered this variable. On the other hand, in utero effects of maternal active smoking could be a possible confounder relative to associations between postnatal maternal smoking and the respiratory system effects in infants that would otherwise be attributed to ETS exposure [1-3]. As can be seen from table 1, however, only 4 studies addressed this particular potential confounder. Item 22 ('others') was added when, in the course of this study, it became apparent that some confounders did not fit the 21 predetermined categories. As indicated in the body and footnotes of table 2, there were too few examples in this category (only 1 or 2 of each of the 5 different factors) to perform any valid analyses on their impact, if any.

Among the 21 potential confounders that we looked at, there was wide variation from study to study in their consideration. Only 7 of the 21 potential confounders (SES, family health history, subject's personal health history, family size, residence location, age and gender) were considered in 50% or more of the 41 studies. This is similar to what was found relative to the confounders considered in the majority of clinical endpoint studies of school-age or older children, i.e. SES, family size, residence location, age and gender. In both sets of clinical studies, the age of the subject and SES were the 2 most frequently considered confounders; addressed in 75-100% of the papers. The confounders that were considered relatively infrequently (in <25% of the studies) or not at all in the epidemiologic studies of pre-school children were other forms of indoor pollution, day care use, animal exposures, stress, dampness/cold, season, occupational exposures, nutritional status of the subject, and maternal smoking during pregnancy. Some of the very same confounders were considered infrequently in the studies of school-age or older children, namely, indoor pollution, day care use, animal exposures, stress, dampness/cold, season, occupational exposures and nutritional status [4].

Table 2 showed that there is wide variation from study to study in the array of confounders taken into consideration; a situation similar to that observed by us previously in studies of school-age children [4]. When evaluated on the basis of number of confounders considered per study (table 3), the representation in each paper is poor. Only 3 of the 41 preschool studies considered more than 10 of the 21 potential confounding variables, with the largest representation of confounders being 16 in 1 study. The situation was similar in studies of older children, where 7 of 45 papers considered 10 or more confounders, with the largest number of confounders considered being 12 [4].

The clinical endpoints were validated by medical records or physical examination in 21 of the 41 studies on preschool children, which is considerably greater than the 8 of 45 noted for studies in school-age children [4]. Nevertheless, it is noteworthy that in almost 50% of the studies, even in preschool children, clinical endpoints were not validated.

In the current report, 12 of the 21 potential confounders were analyzed in detail. Of those that have not been so analyzed, residence location, family size, outdoor pollution and quality of housing were considered in 23, 23, 16 and 9 studies, respectively. Of the remaining variables, animal exposures, stress, nutritional status and maternal smoking during pregnancy were considered in relatively few (1-4) of the papers, while occupational exposures, as in the case of school-age studies [4], were not considered at all.

Of the confounders examined in detail, a very large variety of specific criteria were used to define/determine SES, family health history, personal health history and age, in particular. This lack of standardization among these same potential confounding variables was also noted in our analysis of studies of parental/household smoking in school-age children [4, 5].

Table 12 summarizes our findings with regard to the issue of which confounders appear to be consistently associated with increased risk of respiratory illness in children. They are family health history, young age, male gender, personal health history and, although involving relatively few studies, day care use and season. Of these, family health history, male gender and personal health history were also found to be risk factors for respiratory illness, as well as influencing pulmonary function, in older children [4, 5].

As noted previously, family health history could influence the respiratory system through either genetic or infectious mechanisms [4]. Most of the available studies in preschool children observed no consistent association for SES, artificial feeding and gas fuel use/indoor pollution, or they were inconclusive (due to variable results or small numbers) relative to dampness/cold and heating/air-conditioning. These same factors were either not associated with endpoints or gave equivocal results in studies of school-age children [4].

In addition to a lack of standardization in the types of confounders considered, their specific criteria, the clinical endpoints examined and their validation, there was also marked variation in the statistical methodologies used to adjust for confounding variables in these epidemiologic studies of parental/household smoking in preschool chil-

dren, as was commonly the case with studies in school-age or older children [4, 5].

As has been noted previously [4, 47], confounding variables may account for and/or contribute to effects that are associated with a presumed independent variable such as ETS, even in a dose-related fashion and even when associations between an endpoint and the confounder are not demonstrable. Furthermore, residual bias may persist even after adjustment of a confounder due to misclassification [47]. In addition to their individual influences, several potential confounders may interact with one another and this interaction may be inadequately addressed by standard methods [47].

### Conclusion

While a perfectly designed epidemiologic study pertaining to the effects of parental/household smoking on respiratory illness and disease in preschool children may be difficult, if not impossible, to achieve, our analysis of the relevant studies in this area suggests the need for implementation of certain procedures in future studies. There is clearly a need for more consistent and comprehensive consideration of potential confounders. The po-

tential confounders addressed should not only be those identified herein as having a strong influence on the respiratory system of preschool children but also those that appear to have little effect. For example, while a variable such as SES may have little influence on the incidence of respiratory symptoms and disease in children, it is also possible that the apparent lack of effect observed for SES could reflect the wide variation of criteria and lack of rigor used in its classification. Thus there appears to be a greater need to standardize as well as strengthen the criteria used for the identification of potential confounding variables in general. Furthermore, those potential confounders that have received relatively little attention to date (particularly those that intuitively appear to be important, such as indoor pollution, day care use, animal exposures, nutritional status and maternal smoking during pregnancy) should be considered in future studies. Further analysis should also take into consideration the potential influence of selected combinations of variables as well as their interactions. Finally, in addition to consistent validation of clinical endpoints (which is lacking to date), future studies should consider a standardization of experimental design, the questionnaire employed, the method of gathering information and statistical treatment of the data.

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